UNIVERSIDADE DE LISBOA

FACULDADE DE MEDICINA

BASIC-SELF DISORDERS BEYOND SCHIZOPHRENIA: ULTRA-HIGH-RISK STATES AND PANIC DISORDER

Luis António Proença Duarte Madeira

Orientadores: Prof. Doutora Maria Luísa Caruana Canessa Figueira da Cruz Filipe
Prof. Doutor Louis Arnorsson Sass

Tese especialmente elaborada para obtenção do grau de Doutor em Medicina
Especialidade em Psiquiatria e Saúde Mental

2017

A impressão desta dissertação foi aprovada pelo
Conselho Científico da Faculdade de Medicina
da Universidade de Lisboa
em reunião de 23/11/2016

UNIVERSIDADE DE LISBOA

FACULDADE DE MEDICINA

BASIC-SELF DISORDERS BEYOND SCHIZOPHRENIA: ULTRA-HIGH-RISK STATES AND PANIC DISORDER

Luis António Proença Duarte Madeira

Orientadores: Prof. Doutora Maria Luísa Caruana Canessa Figueira da Cruz Filipe

Prof. Doutor Louis Arnorsson Sass

Tese especialmente elaborada para obtenção do grau de Doutor em Medicina Especialidade em Psiquiatria e Saúde Mental
Juri:
Presidente: **Prof. Doutor José Luis Bliebernicht Ducla Soares**, Prof. Catedrático em regime de tenure e Vice-Presidente do Conselho Científico da Faculdade de Medicina da Universidade de Lisboa
Vogais:

- Prof. **Doutor Carlos Manuel Moreira Mota Cardoso**, Professor Catedrático da Faculdade de Psicologia e Ciências da Educação da Universidade do Porto
- Prof. **Doutor João Eduardo Marques Teixeira**, Professor Associado da Faculdade de Psicologia e Ciências da Educação da Universidade do Porto
- Prof. **Doutor Manuel Gonçalves Pereira**, Professor Auxiliar da Faculdade de Ciências Médicas da Universidade Nova de Lisboa
- Prof. **Doutor Daniel José Branco de Sampaio**, Professor Catedrático Jubilado da Faculdade de Medicina da Universidade de Lisboa
- Prof. **Doutora Maria Luísa Caruana Canessa Figueira da Cruz Filipe**, Professora Catedrática Jubilada da Faculdade de Medicina da Universidade de Lisboa (orientador)
- Prof. **Doutor Miguel Joaquim Santos Lima Oliveira da Silva**, Professor Catedrático da Faculdade de Medicina da Universidade de Lisboa
- Prof. **Doutor António José Feliciano Barbosa**, Professor Associado com Agregação da Faculdade de Medicina da Universidade de Lisboa

Financiada pela Fundação para a Ciência e Tecnologia - SFRH/SINTD/95675/2013 – no âmbito do estatuto de Interno Doutorando

2017

To my family, who fostered me,
my character and resilience

and to my friends
to whom I owe endless support.

Scientific impact and subjective interest

For the author, the choice of the theme presented itself as a fundamental topic for clinical practice, academically linear to his previous studies and an intuitive choice.

A contemporary understanding of the core of schizophrenia, consistent with various neurobiological translational evidences is fundamental, and probably the most important contribution from phenomenological psychopathology. These phenomena occur in Schizophrenic subjects, in their first episode of psychosis, in their prodromal phases and even in Ultra-High-Risk phases. The reputation of this topic stands upon 3 stalwarts: (1) it convenes a new conceptual halo for what it is like to have schizophrenia; (2) it illuminates the subjective world of these patients (*how* they experience) and (3) it might allow early diagnosis and its primary prevention. Yet most importantly its importance stands due to its linear application in clinical practice, with no need for imaging procedures, for learning a particular language (same as the psychopathological examination) and because it is easily taught – having a well-defined epistemology.

It is academically linear. It flows directly from (1) a 3-year Master in Philosophy and Psychiatry where the Master thesis was a selective review of literature under the topic "Appraising Basic-Self Disorders: A Plea Against the Copenhagen Hypothesis" and (2) a training in the Institute of Psychiatry and the OASIS (Outreach and Support Lambeth, Southwark, Lewisham & Croydon) with Ultra-High-Risk subjects (UHR).

Yet most importantly, it was an instinctive choice. The practical uses of Anomalous Self-experiences as risk bearers of schizophrenia troubled the author as he had experienced many of these experiences and schizophrenia had not been diagnosed. Furthering the knowledge on the subjective experiences in UHR and anxious disorders provides detail into the "disparities" and "affinities" that these subjects present vs schizophrenia. Therefore, by fostering the specificity of ASE for schizophrenia spectrum disorders or identifying particular subsets is of key relevance for the use of this model in adolescence and Ultra-High-Risk subjects. In these situations, anxiety is very frequent and could account for psychotic-like experiences or derealisation and depersonalization experiences – similes of ASE and therefore a confounding element.

He believes this research makes a crucial contribution to furthering the understanding of an important dimension of psychopathology in the realms of both the schizophrenia spectrum and anxiety disorders. The manuscript has been prepared according to the Centro Académico de Lisboa style specifications and requirements. The author declares no conflict of interest.

Acknowledgements

This thesis was written in *Centro Académico de Medicina de Lisboa* which comprises a college – *Faculdade de Medicina of Universidade de Lisboa* and a hospital – *Centro Hospitalar Lisboa Norte* (CHLN). It was financially supported by the Fundação para Ciência e Tecnologia – SFRH/SINTD/95675/2013 – in the academic years of June 2013/ June 2014 and June 2014/ June 2015. It also received support from the Maudsley Philosophy Research Group Grant and a Wellcome Trust grant. The latter supported all research performed in the Institute of Psychiatry in London under the main project NEUTOP.

It would be ideal to list all the persons that made this thesis possible but it is unrealistic. Also, but even harder, I would like to name all those that incited me to grow further into the field of psychopathology. Hence everyone I was not able to greet in person – please accept a particularly warm thank you. My choice to name some refers to the standard of their contribution, both distinctive and invaluable:

Prof. Maria Luísa Figueira whose contact was life-changing and from whom, now more than 7 years, I've profited from everlasting support. She encouraged me, provided me input as an expert, chaired and worked with me as a peer in international conferences.

Prof. Louis Sass, for his care, support and supervision in the thesis. All three were impressive and inspiring. Indeed, I consider myself particularly lucky in having such close supervision from such a warm-hearted person.

Prof. Daniel Sampaio, for numerous supports, for his guidance in executive and scholarly matters, and, particularly, for his protection and safeguard that allowed me the time to research and to write this thesis.

Prof. Giovanni Stanghellini, for his enthusiasm and knowledge that contributed vastly to what I know today in Psychopathology.

Prof. Michael Musalek for his compassion and inspiring idea that the "how" is far more important than the "what" in psychopathology.

Prof. Tim Thornton and Prof. Gloria Ayob, who supervised my Master in Philosophy and Mental Health – my first venture into the vast field of Psychopathology.

Dr. Paolo Fusar-Poli for his contribution to my personal growth in the field of research in Psychiatry.

Dr. Ilaria Bonoldi and **Dr. Matteo Rocchetti** for their kindness, understanding and genuine support during my stay in London.

Prof. Julie Nordgaard, for introducing me to the self and whose contributions to the field of phenomenology and psychopathology are immense.

Dr. Monica Salgado, whose friendship and wisdom allowed me to keep my sanity in so many circumstances.

It should also be stated that much of the research material herein was presented in several international meetings. These permitted profiting from supervening (vital) debates and from immensely valuable suggestions and comments.

Lastly, and above all – I thank all patients and volunteers for their collaboration in this research whom I hope will benefit from its results.

Publications that resulted from the Thesis

Primary

1. Madeira, L., Bonoldi, I., Rocchetti, M., Samson, C., Azis, M., Queen, B., et al. (2016). **An initial investigation of abnormal bodily phenomena in subjects at ultra high risk for psychosis: Their prevalence and clinical implications**. *Comprehensive Psychiatry*, *66*, 39–45. http://doi.org/10.1016/j.comppsych.2015.12.005

2. Madeira, L., Bonoldi, I., Rocchetti, M., Brandizzi, M., Samson, C., Azis, M., et al. (2016). **Prevalence and implications of Truman symptoms in subjects at ultra high risk for psychosis**. *Psychiatry Research*, *238*, 270–276. http://doi.org/10.1016/j.psychres.2016.02.001

3. Madeira, L., Carmenates, C., Costa C., Linhares L., Figueira, M.L., Sass L. (2016) **Basic-self disturbances beyond schizophrenia: "discrepancies" and "affinities" in Panic Disorder** *Psychopathology* (submitted in November 2016)

Secondary

- **Madeira L Figueira ML** Chapter **An Experiential Approach to Dissociative Disorders** in the Book **An Experiential Approach to Psychopathology** – Phenomenology of Psychotic Experiences Dissociation Springer 2016 (ahead of publication)

- **Madeira L Bonoldi I Young A Nelson B** Chapter **Psychosis High Risk states** Book **Oxford Handbook of Phenomenological Psychopathology** Oxford University Press 2016 (ahead of publication)

Abbreviations

Abnormal bodily phenomena (ABP);

Abnormal Bodily Phenomena questionnaire (ABPq);

Anomalous Self-Experiences (ASE);

Cambridge Depersonalization Scale (CDS)

Examination of Anomalous Self Experiences (EASE);

Prominent Abnormal Bodily Phenomena (proABP);

Ultra High Risk (UHR);

Ultra High Risk subjects with Truman symptoms (UHR-TS+);

Ultra High Risk subjects without Truman symptoms (UHR-TS-)

Ultra High Risk subject with prominent ABP (HRproABP+)

Ultra High Risk subject with no prominent ABP (HRproABP-);

Comprehensive Assessment of At-Risk Mental States (CAARMS);

Matched healthy controls (HC);

High Clinical Risk (HR);

Positive and Negative Syndrome Scale (PANSS);

Social and Occupational Functioning Assessment Scale (SOFAS);

Matched healthy controls (HC);

Truman symptoms (TS);

Panic Disorder (PD);

Index

Index of Tables

Index of Figures

General Abstract

This thesis investigates Anomalous Self-Experiences (ASE) testing new ways of their symbolization (e.g. Truman Symptoms), extending the detail of their subsets (e.g. abnormal bodily experiences) in Ultra-High-Risk (UHR) and further isolating them in new settings, such as anxiety disorders. The first aim was to study Truman Symptoms (TS) including their presence in UHR, their clinical implications and their relation with ASE. The second aim was to study the Abnormal Bodily Phenomena subset of ASE in UHR and to determine their clinical implications. The third aim was to identify if ASE occurred in Panic Disorder, to characterize their profile in this category considering possible differences from schizophrenia.

Anomalous Self-Experiences are the most important contemporary conceptual and empirical research topic in the field of Schizophrenia. The set of these subjective phenomena constitutes particular traits of schizophrenic subjects which are present in the 1st episode of psychosis, in prodromal and in Ultra-High-Risk states. Outstandingly, such enquiries have raised the standard of the psychopathological examination as they've endorsed reconsidering subjective phenomena to increase validity of a psychiatric category without sacrificing reliability. This constituted the first step to sanction a new set of enquiries which contemplate other subjective phenomena in schizophrenia and also recognize the possible role of psychopathology of subjectivity in other disorders. This thesis stands upon the latter phenomenological entreaties in three separate approaches.

It starts by taking on Truman Symptoms, a contemporary way of symbolizing depersonalization/derealization experiences, to identify their relevance in UHR and considering their relation with ASE. TS seem to represent a fresh cultural symbolization of the initial phase of psychosis and yet no empirical enquiry has set their bearing in the risk of psychosis, found possible analogies to ASE or a relation with other clinical measures. It continues by addressing the subset of bodily ASE, of which the relevance in a schizophrenic sample has been recently reconsidered. Deploying a new instrument – the Abnormal Bodily Phenomena Questionnaire – it examines the UHR states drawing the relation of these unique subjective elements with established ASE and other clinical measures.

Lastly it probes the presence of ASE in a well-established, almost archetypal, nosological category of anxiety – Panic Disorder – aiming to contribute to the characterization of the psychopathological forms of their subjectivity. Such enquiry seems fundamental to the use of ASE in UHR populations where anxious settings are extant and therefore identifying particular clusters which could be representative of more severe disturbances of "basic-self" as crucial for their clinical relevance.

Resumo em Português

Perturbações do Self-Básico para lá da Esquizofrenia: Estados de Ultra-High-Risk e Perturbação de Pânico

Esta tese representa uma parcela do esforço atual no âmbito translacional da fenomenologia na sua aplicação translacional para as classificações tendo como objetivo recuperar o significado clínico das experiências subjetivas no diagnóstico e intervenção terapêutica da esquizofrenia e Perturbações de Ansiedade. Desde o DSM-III que a procura de fiabilidade favoreceu os sintomas objetivos e a operacionalização progressiva das categorias psiquiátricas traduzindo-se numa abordagem simplicista da complexidade da experiencia humana. Isto originou vários problemas de validade dos sintomas utilizados e conduziu a limitações graves à psicopatologia e nosologia da Psiquiatria. Em particular salienta-se o facto desta tese se centrar na tentativa de encontrar um core para a esquizofrenia – hoje uma categoria heterogénea construída por vários consensos e com grande variabilidade relativamente aos sintomas inaugurais. O paradigma de perturbações do *Self,* tão importante para a esquizofrenia e tal como utilizado nesta tese, inscreve-se desde contribuições seminais até aos estudos mais recentes na área (quer clínicos quer translacionais). A natureza das perturbações do *Self* como "traço" condicionou a sua utilização para lá dos diagnósticos de psicose e esquizofrenia considerando-se a sua presença em estados prodrómicos e Ultra-High-Risk. De facto, após estes desenvolvimentos, novos cluster de sintomas emergiram e estão a ser testados como marcadores de Episódio Psicótico, tais como os Sintomas Truman e as Perturbações do Self-Básico.

No entanto, a introdução destes novos componentes na clínica (nomeadamente a sua inclusão no exame psicopatológico) depende de mais estudos capazes de os clarificar do ponto de vista fenomenológico e clínico. O objetivo fundamental desta tese é procurar perceber e caracterizar as experiências anómalas do Self-Básico, em pacientes com P. Ansiedade e em indivíduos em estado Ultra-High-Risk para psicose. Em primeiro lugar, utiliza-se o novo conceito de Sintomas Truman como uma forma de representar experiências anómalas do *Self* num grupo de Ultra-High-Risk. Em segundo lugar, detalha-se o conjunto de experiências anómalas do *Self* do subtipo corporal, utilizando um questionário próprio, Anomalous Bodily Phenomena Questionnaire (ABPq). Por último examinam-se as

experiências anómalas do *Self* numa amostra de doentes com P. Pânico procurando iluminar a fenomenologia destas experiências subjetivas na ansiedade e identificar clusters das mesmas com maior incidência no espectro da esquizofrenia ou, pelo contrário, aqueles que ocorrem em formas patológicas de ansiedade.

O primeiro braço do estudo compreendeu a prevalência e especificidade dos Sintomas Truman numa amostra de pessoas em Ultra-High-Risk. Obteve-se como resultado serem um marcador fenotípico destes estados (UHR). O argumento principal consiste em que os Sintomas Truman podem ser um sintoma nos estados UHR e contribuir para identificar um subgrupo de pessoas que têm psicopatologia mais grave. Nesta amostra não se encontrou relação entre os Sintomas Truman e as Perturbações do *Self* ou mesmo com a despersonalização em geral (medida pela escala de Despersonalização de Cambridge) mas especulou-se que poder ser um falso negativo em face da reduzida dimensão da amostra estudada. Tendo-se registado uma significativa correlação entre a Escala de Despersonalização de Cambridge e a escala Examination of Anomalous Self Experiences considerou-se a necessidade de atender as "Perturbações da Experiência do *Self*" de experiências de despersonalização e desrealização sem outra especificação. Uma sobreposição limitaria o uso de narrativas de experiências de desrealização e despersonalização para determinação de experiências anómalas do *Self*, uma vez que estas seriam transnolosológicas e não teriam um significado para o diagnóstico de esquizofrenia.

No segundo estudo em que se avaliaram Experiências Corporais Anómalas na população de Ultra-High-Risk, foi possível encontrar várias destas experiências na amostra de UHR – saliente-se que 14 em 26 indivíduos as referia de forma proeminente. Isto permitiu especular que possam ser também marcadores fenotípicos de vulnerabilidade de psicose. Porém, mais de 30% dos indivíduos UHR não mostraram ABP, o que deu uma robustez maior à noção prévia de que estes estados são heterogéneos, incluem várias co-morbilidades e podem ser apresentações inaugurais de vários diagnósticos condicionando vários desfechos clínicos. A presença de ABP não diferenciou a amostra de UHR em scores das escalas SOFAS ou PANSS, e os sujeitos com ABP proeminentes apresentavam um score de CAARMS inferior aos restantes. Estes resultados podem resultar de se tratar de uma amostra pequena com baixa significância estatística, sendo necessários estudos maiores para averiguar o seu significado. Porém podem também significar que o questionário ABPq avalia fenómenos diferentes daqueles a que actualmente se aplica, ou seja, nos de elevado

risco de psicose (incluindo os fenómenos corporais na CAARMS). Nesta amostra os indivíduos com ABP proeminentes não tinham scores EASE significativamente superiores, podendo significar avaliarem aspetos diferentes da experiência do corpo ou apenas um falso negativo.

Os resultados dos doentes com Perturbação de Pânico da amostra mostraram que estes experienciam também perturbações do *Self*-Básico, apresentando valores da EASE significativamente superiores àqueles reportados em estudos com doentes com Perturbação Bipolar e outras perturbações fora do espectro da esquizofrenia. Foi possível considerar três possibilidades: (1) que as Experiências anómalas do *Self* na Perturbação de Pânico e na Esquizofrenia são fenómenos idênticos, tendo a ansiedade grave como denominador comum; (2) que as Experiências Anómalas do *Self* na Perturbação de Pânico e na Esquizofrenia são fenómenos idênticos mas apenas superficialmente – e que a entrevista EASE não é capaz de as distinguir; (3) clusters diferentes de Experiências Anómalas do Eu podem ocorrer na Esquizofrenia e a na Perturbação de Pânico, com padrões específicos apenas visíveis num exame cuidado e detalhado. Esta investigação permitiu verificar porém que determinadas anomalias da experiência do *Self* são raras na Perturbação de Pânico, particularmente aquelas que correspondem a uma distorção profunda na vida subjetiva – no plano neurobiológico consideradas como a base da desintegração da perceção em doentes com ou em risco de esquizofrenia. Esta constatação sugeriu que as anomalias da experiência do Self encontradas na Perturbação de Pânico pudessem ser de um tipo diferente, provavelmente envolvendo fenómenos secundários ou defensivos e formas mais simples de despersonalização e desrealização.

A inferência principal resultante da análise de resultados da amostra de doentes com P. Pânico é a de que possam existir especificidades na expressão da sua ansiedade que eram, até hoje, desconhecidas. É possível especular que traços e características subjetivas na Perturbação de Pânico (que a Psiquiatria desconhecia), possam explicar o porquê de estes pacientes não responderem ao tratamento psicofarmacológico inicial e serem referenciados a um contexto hospitalar (necessitando de um tratamento específico). Por último, e de acordo com os resultados já obtidos inicialmente na amostra de UHR, a existência de correlação entre a EASE e a CDS na amostra de indivíduos com Pânico reforçou a relação entre as experiências de despersonalização e as anomalias da experiência do *Self*. Mesmo assinalando

a sobreposição dos itens da entrevista, os resultados obtidos reforçam a necessidade de um maior detalhe na descrição destes fenómenos.

Os resultados desta tese são, porém, limitados pelo tamanho da amostra e dois dos estudos que a compõe (com amostra de UHR) devem ser considerados como exploratórios. Se considerarmos o tamanho da amostra, o processo de seleção dos indivíduos incluídos na amostra de Pânico e o facto de terem sido utilizadas só duas clínicas de UHR, devemos pressupor que os resultados possam ser positivos ou negativos. Destacam-se outras limitações importantes, nomeadamente a falta de estudos de follow-up e a não utilização de um grupo de controlo clínico (por exemplo, de Perturbação Afectiva, Perturbação de Ansiedade ou de Perturbação de Personalidade), as quais sendo ultrapassadas, permitiriam definir melhor (1) a relevância clínica dos sintomas Truman e das anomalias da experiência corporal e do *Self* para os estados UHR bem como (2) as anomalias da experiência do *Self* na Perturbação de Pânico. Por último, não foram avaliados os impactos da utilização de drogas ou de substâncias ilícitas que também poderiam influenciar os resultados aqui obtidos.

Chapter 1: A Selective Review of the Conceptual Field of Research

1. The self and its disturbances

1.1 Seminal contributions to the idea of Self

The understanding the Self has been a long-lasting pursuit of Philosophy, Psychology, Psychiatry and more recently, neurosciences. It is therefore a strong field of translational research where the entails of each paradigm are attempted to its conceptual heterogeneity and variegated use of the Self in practice (Sass et al. 2011). In Philosophy, the descriptions of the Self run from Aristotle' till today and major philosophers have plunged in its matters. The XIX century allowed another stance, from psychology, important as it focuses in subjectivity and promotes introspection as clinically important and an instrument for collecting data (Sass et al. 2011). In Psychiatry, the Self and its disturbances has been particularly explored in many seminal contributions where we find descriptions of mental symptoms and mental disorders involving the self as in Pierre Janet, Hans Gruhle, Joseph Berze, Eugène Minkowski, Ludwig Binswanger and Wolfgang Blankenburg. In the field of Neurosciences, there has been extensive input risen along the last 4 decades and these efforts aim to present us with a translational effort from specific disturbances of the self to areas of the brain which can constitute disturbances (Kircher & David 2003) (S. Gallagher 2011).

Tackling the Self in Philosophy brings up the ideas of "self-consciousness" and "self-reflection". The former meaning finds its way back to Aristotle's idea of "memory" – knowing oneself by past actions and life and to narrative dimension of self-awareness. The second also takes into account the Stoics idea of Phantasiai – the *individuation* of experiences and – hegemonikon – the *mineness* of experience (Sandbach 1989). The possibility of privately meeting with oneself was presented by Plotinus (Rappe 2007) and later by Saint Augustine worked over the concept of "*space of retreat*". A major contribution was made by Victor Frankl notion of Self that encompassed (1) the presence of double structure (being subject and simultaneously object of experience), (2) the reflexive nature consciousness and a (3) sense of familiarity ((Frankl 1975). Yet far before that, Descartes notion of *res-cogitans* would add and revolutionize use of the word Self by the construction

mind-brain dichotomies. The discussion thenceforward was now on the nature and properties of the *empirical* (physical) and of the *transcendental* (mental) self. Considering all the contributions is out of the scope of this chapter (but can be found in (Kircher & David 2003; Kircher & David 2009)). Yet, to clarify the ideas of Leib and Korper and of the transcendental structure of subjectivity Plessner, Buytendijk, Husserl, Merleau-Ponty and Sartre are revisited in the next sections.

Plessner was the first to propose the distinction between *leib* and *korper* in respect to anthropological distinction between animals and humans (see Kruger discussion on the origins of the terms (H.-P. Krüger 2010)). Later on, the terms Leib/Leibsein/Leiblichkeit used in philosophy by Gernot Bohme, Edmund Husserl and Maurice Merleau-ponty to affirm the importance of considering what it is *"to be"* a body. That referred to the capacity of subjectively appreciating the body as "alive and living", its pre-reflexive cognitive and affective mode of experiencing of oneself and the world (both immediate and intentional). In other words, this way of experiencing oneself is constituted by the "sensorimotor subjectivity: a situated, forward-flowing, living organismic body of a suitable degree of neurobiological complexity" (Maiese 2011). Paradoxically, while in such a state the person is not explicitly aware of him/herself - this state is not reflexive or self-conscious (see further discussion in (Carman University of Arkansas Press 1999)). Indeed the conscious experience of what it is like *"to have"* a body constitutes the notion of *korper* – or – the body-as-objectively-experienced. It refers to the objectified and physically bound properties of the body. Together *leib* and *korper* can be portrayed in the movement of one's left hand to touch the right hand – the latter is experienced as physical whilst the first is providing the experiential awareness of the other.

The phenomenological authors also support the possibility of a transcendental structure of subjectivity – ontological structure of the perception of reality which includes properties such as spatiality, temporality and bodily awareness, self-awareness and other–awareness. Merleau-Ponty proposes that these formal pre-reflexive ways of grasping reality lose their implicit statuses and become explicit when disturbed (as it could be in the case of mental disorders) "of the intentional threads which attach us to the world...when feeble those intentional threads (time, body, and immersion in the world) become visible" (Merleau-Ponty 1962). Here is briefly discussed all but the self-awareness as it is part of the major discussion of this thesis.

Spatiality as a transcendental structure is not the experience of space (as a phenomenon) but the way one is, at each moment, distinctively situated and set in the world. Such is the notion of "*prenoetic spatiality that is never fully represented in consciousness or captured by objective measurement*" (S. Gallagher 2006) rather a framework which allows me to see the world at-hand in respect to its relation with oneself and one's body. Spatiality involves various forms of being in space (tridimensional, natural orientation, lived, historical, humoral space). The concept of hodological space (Lewin 2013) is fairly illustrative of the way that factual, topological, physical, social and psychological circumstances affect space experience.

In respect to temporality, a similar discussion is raised on how it is involved in the perception of the world. Proposed by Kant, such experience of "time is nothing else than the form of the internal sense, that is, of the intuitions of self of the internal state. For time cannot be any determination of outward phenomena. It has to do neither with shape nor position, on the contrary, it determines the relation of representations in the internal state." (Kant 2013). If "temporality" is adequate then the pre-reflexive involvement in microstructure of experience allows for time to flow unrestricted – "every time that we are absorbed in what we are doing, and may even reach the climax of "flow experiences" (M. Csikszentmihalyi & I. S. Csikszentmihalyi 1992) where the "sense of time is lost in unimpeded fluent performance". Yet also it allows for the perception (of the world) to be "future oriented" and for adequate sorting of "before/after relationships" (Wyllie 2005). But one can leave such state, as in tedium and boredom where we are forced to become aware of time passing. Further disturbances in mental disorders lead to changes in the awareness of lived time (explicit forms of temporality) (Fuchs 2005b), to an increased or decreased "availability of the world" and even, as in schizophrenia, to novel ways of being in the world (Stanghellini et al. 2015).

The pre-reflexive bodily awareness involves the previous discussion on "leib" and "korper". Present conceptualization suggests that the body is also involved in "sense-giving" and that the perception of reality is beforehand integrated in a corporeal scheme. Such "engaged epistemology" is used to apprehend some of the features of delusions which were paradoxical if used in the previous estranged understanding of world relation (Gipps & K. W. M. B. Fulford 2004). But the bodily pre-reflexive awareness of the world is also related to the "experience of possibilities" and to the "intentional arc".

The relevance of intersubjectivity in the ontological structure of reality can be pointed in the possibility of synchronization, an eccentric position on reality and a unique form of apprehending the body. First, the contact with others allows the subject to become "dialectically synchronized" that otherwise would experience "lived time" detached from "the micro-dynamics of everyday contact imply a habitual synchronization… basic feeling of being in accord with the time of the others" (Fuchs 2005b). This synchronization not only regards time but also all the remaining forms of structure of subjectivity – such attunement with the world in general is fundamental. In the second is relevant the ontology of the body-for-others, the encounter with the other is essential to find an "object-to-subject" relation which allows me to "appear/become visible/objectified" - If, therefore, *being-looked-at*, apprehended in all its purity, is no more connected to the *body* and *the Other* than my consciousness of being a consciousness (in the pure effectuation of the *cogito)* is connected to my *own body* - then it is necessary to consider the appearance of certain objects in the field of my experience (in particular the convergence of the Other's eyes in my direction) as a pure *monition*, as the pure occasion for the realization of my being-looked-at (Sartre 1943). This synthetizes this experience of the body as available to the subject.

1.2 The Self in Psychiatry

The Self in Psychiatry has been used epistemologically in the creation of biological and psychosocial models for psychiatric categories and also used as constitutive phenomena. Drawing from the conceptual heterogeneity, the "disturbances of self" are vast and they are used to enlighten complex situations as (1) psychopathology of Schizophrenia (loss of self), (2) multiple personality (and other dissociative experiences) and (3) passivity experiences (also part of experiences in schizophrenia). The first two can be tracked back to Kraepelin discussing distinctive conceptions of the disturbances of the self from dementia praecox (5th edition), changes in self-awareness (6th edition) and depersonalization and multiple personalities (8th edition) – further discussion by Berrios in (Kircher & David 2003)). The third was discussed by Bleuler and includes the experiences of "clouding of thoughts", the nosology "twilight state" and the psychological capacity of "self-awareness" (Bleuler 1924).

Jaspers contributed significantly to the self as psychopathological phenomena by dedicating an entire chapter of his "General Psychopathology" to both changes in the awareness of the self (allocated in activity, identity and unity) and the disorders of self-reflection (disturbances of instinct, bodily function and compulsive phenomena) (Jaspers 1997). Scharfetter further detailed such approach to ego-pathology in 5 basic dimensions (vitality, activity, consistency/coherence, demarcation and identity) probing their presence in empirical studies (Scharfetter 1981) (Scharfetter 1995). Another conceptual concept of the meaning of the Self was related with the notion of "coenesthesia" which denoted bodily experiences that would not fit within the 5 Aristotelian senses (Reil & Hübner 1794),accepted as a direct access to perceptual information and to be given the same importance as ordinary senses. The relevance of disturbances of the self in schizophrenia.

1.3 Embodiment and Enacted Knowledge

Further delving into the disturbances of the self implicates knowing the concepts of "embodiment" and "enactment" which today infuse the discussion of "basic self disturbances". They stand upon a critical appraisal that the "neural system" must be more than just a sensor / processor of external and internal stimuli. Such understanding is in sharp contrast with the "Brainbound model" which has constituted a "Cartesianist" approach to brain-body and main model of understanding of human experience and behavior until

recently (see (Clark 2008)). Distancing itself from such materialist and dualist accounts, the embodied model supposes that the body (beyond the brain) is also sthece of knowledge both in the *form* it assumes and its *dynamics*. This view is expressed both in seminal works of phenomenologists as in Maurice Merleau-Ponty (Merleau-Ponty 1962) and in more specific contributions by Lawrence Shapiro, Shaun Gallagher (S. Gallagher 2011), Francisco Varela and Evan Thomson (Varela 1993) and Michelle Maiese (Maiese 2015a). They propose that (1) the body has a constitutive role in cognitive processing, (2) there is an "engaged epistemology" where the bodily shape and form are relevant for assessing and accessing the world (S. Gallagher 2006) , (3) the body as the means of a "living mind" – mindedness is spread out through the body (Maiese 2015a; Hanna & Maiese 2009). Maiese further clarifies that the body entails both "necessity" and "completeness" supporting that "we are always and necessarily conscious *in and through* the living bodies; and it is only complete *minded animals* that are intentionally directed, not their body parts alone, and not even their brains alone" (Maiese 2015a).

From the ideas of embodiment, one can easily draw the idea of enactive access to the world where the brain is (1) not impassively receiving external stimuli in which it cognitively elaborates but (2) previously bodily meaningful stimuli and (3) that the body itself creates and maintains meanings that are part of the individual identity ((E. Thompson 2007)). This particular strand of enactivism (embodied knowledge) was used to characterize the role of emotions, moods and existential feelings structuring and informing the person's sense of its relation with the object or situation he's in. ((Ratcliffe 2008; Maiese 2015b)). As a whole, the enactive and cognitive knowledge are complementary in terms that in each situation where enactive information (action) fails the cognition takes command.

As Maiese emphasises, the embodied engagement and enactment seem responsible for a "basic sense of self" - constituting both the basis of a living body and the condition of a lived body (Maiese 2015a). When the person is able to intuitively navigate and adapt to each situation, meaning when in full performance, they also experience a feeling of being and their own sense of self.

1.4 Louis Sass and the Copenhagen School

The most relevant operationalization of the self was laid out by Joseph Parnas (Bovet & Parnas 1993), Louis Sass (Sass & Parnas 2003) and Dan Zahavi (Zahavi 2008) and was further supported by various studies arising in the Center for Subjectivity Research (Copenhagen). It includes a theoretical and empirical proposal for the concept of Self that comprises an *inverted pyramidal structure* standing upon "the basic self" – a pre-reflexive engagement, enactment and synchronization with the world. Such "basic level of the self" is key to understanding schizophrenia and various other authors provided inputs to it, particularly Giovanni Stanghellini (Stanghellini 2013) and Thomas Fuchs (de Haan & Fuchs 2010). The "basic level of self" or minimal self involves the subjective self-experience in routine performance which is not available to consciousness and therefore only revealed in specific psychopathological conditions. It is part of three *levels* (basic, reflexive and narrative) of self-experience:

A first level encompasses "the minimal Self" ((Cermolacce et al. 2007; Legrand 2007)) and encompasses pre-reflexive experience, meaning and synchronization with others and the world. In the core concept are ideas of "*ipseity*" (a non propositional acquaintance with oneself), *self-awareness* (ecological awareness of the position in the world and awareness of the environment), vital feelings (Scheler in (Kircher & David 2009)), "*self-affection*" and *affect resonance* (possibility for interpersonal synchronization); *agency* (imbued intentionality), and *self-continuity* (retentional-protentional unity of internal consciousness and temporal coherence). The "minimal self" functions as a basic embodied and enacted relation with the world relieving the person of much of the effort of relating and understanding reality – it works through an intuitive and transparent activity. Disturbances in this level make the subject aware of being separate from oneself or of a sense of unfamiliarity or unreality of the environment. Also such immediate understanding allows the subject to act upon his perceptual experiences without cognitive effort. So beyond allowing a "pathic" experiential feature the minimal self refers to a "gnostic" pre-reflexive or experiential meaning that imbues experience before any cognitive enterprise.

Hierarchically a second level of self materialises, built over the previous, but different in nature as the subject is aware of it and willingly uses this level for himself. It includes functions of *self-reflection*: ability to build judgments and beliefs (not only cognitive) on oneself and the world; of building of a *body image*: the reflexive concept of oneself; and *perspective taking* – the possibility to take an alocentric assessment of reality (Raballo 2012). Disturbances of such level might occur due to changes in proper thought but also due to changes in the other dimensions of self-experience. Examples of these are the descriptions of hyper-reflexivity and abstract idealization ("a kind of spiritual or intellectual utopian ideology, detached from concrete daily interpersonal life" (Stanghellini 2004) in Schizophrenia.

The third level of the "self" includes notions of cohesive judgments, attitudes and memory arrangements that add up to the experience of having a biography and to the possibility of portraying oneself through narratives (P. H. Lysaker & J. T. Lysaker 2008; I. Gallagher 2000) (autobiography). This narrative dimension of Self-concept is expressed in the patient's self-portrayal and set of attitudes. Cognitions and experiences are incorporated in one's experience of time and space. Knowing one's past and knowing one's changing autobiography leads to a singular type of narrative sense of continuity. The second and third level of self-experience can be grouped into the idea of narration.

Another relevant experiential feature of the self is the physical dimension including Sartre's notion of Korper (see more in (Stanghellini, Ballerini, Blasi, et al. 2014; H.-P. Krüger 2010)) and the way we capture the body as *corporal* (as is studied by natural sciences as anatomy). The physical body is many times a background experience that we are not aware of but sometimes comes out to the centre and leading us to see ourselves as materialized. It becomes explicit when under physical diseases (e.g. influenza) where it resists movement and is perceptualized. Similar experiences occur in the experience of shame where rich descriptions of reification and exposure detail how the body becomes an object to oneself.

These ideas have been used to describe many of previously ineffable and incomprehensible experiences in Schizophrenia Spectrum Disorders (Raballo 2012; Postmes et al. 2014; Parnas & Henriksen 2014). For instance (see below for a detailed depiction) the appearance of hyper-reflexivity as (1) involuntary process to deal with increased experiential data which were previously transparent; (2) primary activation of the mind towards itself because of

alienation; (3) defensive compensatory forms to the loss of control over the structure of the self. This would lead all to an experience of self-alienation, depersonalization and to delusional systems.

1.5 The inputs from neurosciences

The descriptive nature of the concepts previously discussed has been gradually transformed by subsequent translational studies into a neurobiological paradigm. These efforts are supported in several models of psychological development ((Piaget & Inhelder 2008; Postmes et al. 2014); (Stern 1998; Rochat 2009)), which materialize the "basic self" in crucial sensory and motor functions. It takes up on contemporaneous cognitive science the idea that actions and perception are interdependent in the constitution of experience ((I. Gallagher 2000; Gallese & Sinigaglia 2010; Merleau-Ponty 2013; Noë 2004)) and that early on disturbances of these occur in persons who later develop schizophrenia ((Erlenmeyer-Kimling et al. 2000; Fis et al. 2008; Schenkel & Silverstein 2004; Sørensen et al. 2010). Yet only few studies have delved into these matters: (1) the group of Joseph Parnas (Parnas et al. 1996), (2) the group of Postmest (Postmes et al. 2014). Borda and Sass further pin-point the shortage of research on the association between schizophrenia-like disturbances of core-self experience and neuropsychological factors (see more in (Borda & Sass 2015; Sass & Borda 2015)). They go further grounding the neurological correlates of primary and secondary functions (and experience) of the self. The primary phenomena (disturbed grip on the world, primary forms of hyper-reflexivity and primary diminished self-presence) would be related with a disturbed organization and integration of perception particularly intermodal integration of motoric, proprioceptive, kinesthetic processes ("perceptual dys-integration"). Otherwise the secondary forms of disturbed self-experience are related with hypoactivity of the central executive network, and hyperactivity of Default-Mode network (DMN) and with salience network dysregulation.

Sass and Borda further detail the neurobiology underlying each of the disturbances of the self in schizophrenia:

1.5.1 Primary Factors

The disturbed "grip" or "hold" on the world: deficits in context processing and abnormal discrimination between familiar and strange stimuli leading to a perceptual disorganization and disintegration ((Martin & Pacherie 2013; Sass 2004)). Disturbances of "Perceptual organization" which entail incapacity to structure stimuli ((Uhlhaas & Silverstein 2005) and of "Perceptual Integration" which refer to a disturbance of intermodal synthesis (Postmes et al. 2014). Both have been found disturbed in schizophrenia samples and ground various deficits on these subjects ((Uhlhaas & Silverstein 2005; Phillips & Silverstein 2003; Postmes et al. 2014)). Such disturbed evaluation of context and between external and internal stimuli leads to an unstable reality that lacks clarity and in which the subject's feeling of bodily presence is severely disturbed

Automatic or "Operative Hyper-reflexivity" referring to the subject feeling that trifle elements of reality become salient and in need of reflection – normal sense of oneself requires that consciousness is at least partially turned off. This experience is conceived as resulting from a disturbed perceptual intermodal integration (as before) but also, and particularly, the inability to "triangulate" all sensory inputs (afferent/body ownership) from his self-in-action (efferent/body agency) (Gamma et al. 2014; Jeannerod 2003; Parnas et al. 1996; Schwabe & Blanke 2007; Tsakiris et al. 2007; Tsakiris 2010; van den Bos & Jeannerod 2002; Wylie & Tregellas 2010). Neurobiological evidences for disturbance of body ownership point to disturbance of bottom-up multisensory integration and areas such as right temporo-parietal junction (TPJ) and posterior parietal cortex ((Ehrsson et al. 2005; Tsakiris et al. 2008)). These areas together with the somatosensory cortex and the insula are responsible for the neuronal representations of a bodily self (see more in (Borda & Sass 2015)).

"Primary diminished Self Presence" (diminished self-affection) which refers to the loss of being present as living and being a unified subject of awareness or agent of action. It is in close relation with the previous two experiences (the subject can no longer take for granted his selfhood while so many tacit experiences become salient and explicit) and yet it goes beyond the sense of ownership and agency to the capacity to distinguish oneself from others ((Herrera et al. 2006; Lallart et al. 2009; Riva et al. 2014; Zahorik & Jenison 1998)). The

neurobiology of this disturbance are similar to the previous and yet also refer to areas of visuospatial organization ((Lallart et al. 2009)).

1.5.2 Secondary Factors

Reflective (or secondary) hyperreflexivity refers to another form of overthinking by directing attention to what would normally be experienced as part of oneself – moving focus from the explicit world to the implicit dimensions of experience. Various negative (removal from the world by being too fatigued and therefore inability to attend to reality) and positive (derealization) symptoms in schizophrenia are taken as secondary to hyper-reflexivity (whether primary or secondary). The Default-Mode Network (DMN) is involved in "self-referential" tasks and was shown to be active in schizophrenia even when it would be naturally suppressed (as in exterior oriented activity). Various medline cortical structures were shown to be related to the DMN (R. J. Murray et al. 2012; Northoff et al. 2006; Qin & Northoff 2011; van der Meer et al. 2010) and are traditionally considered part of the "neural circuitry of self (Brent et al. 2014). Altered salience of interoceptive stimuli could in fact explain some of the positive symptoms in schizophrenia such as hallucinatory experiences (Manoliu et al. 2014; Jardri et al. 2013).

Secondary diminished self-presence – it refers to the intentional or defensive process of diminishing sense of existing or being an agent of action. This experience seems also related to hyperactivation of the Default-Mode Network (DMN) with hypoactivation of Central Executive Network and diminished emotional processing of external stimuli – the salience network (Moran et al. 2013; Nekovarova et al. 2014; Nygård et al. 2012) – the loss of emotions and of feelings of estrangement or detachment from their own mind and body (Sierra & David 2011). These changes are interesting both in schizophrenia (considering the possibility that psychosis involves severe stress levels and the persistent idea of not being able to cope) and in depersonalization post-trauma (either acute or continuous) – all this seems to motivate a secondary form of self-objectification and withdrawal.

Secondary disturbance of "grip" – refers to the incapacity to coherently deal with the foreground stimuli – the incapacity to distinguish between relevant and non-relevant stimuli and the development of rigid attention and focus. Such has been conceptualized as "the abnormal salience hypothesis" where stimuli usually in the background come forward and

interfere with those of the foreground – attention becomes disturbed either by the subjects inability to focus or becoming abnormally focused on specific stimuli (Fletcher & Frith 2008) (Kapur et al. 2005; Kapur 2014; Nelson, Whitford, Lavoie & Sass 2014a; Matussek 1987; Postmes et al. 2014; Hemsley 2005; Hemsley 1976; Hemsley 1998). The ability to focus is akin to the capacity to convey objects and persons their affordances (their importance in the subject's experiential world) – see more in (Gibson 2014). It is difficult for the subject to navigate in a world where everything is deprived of their personal meaning (Sass & Pienkos 2015) and it is the perfect ground for the formation of strange perspectives on the world (Sass & Byrom 2015). The dys-regulation of salience network has been extensively appraised and appears to involve the Central Executive Network (hypo-activity) and Default-Mode Network (DMN) (hyperactivity). This pattern is related with unfocused/mind-wandering states and introspection – indeed, introspection in non-psychiatric conditions has constituted a field of research for psychotic-like conditions (Hunt 1976; Sass, Pienkos & Nelson 2013).

2. Psychosis High-Risk States: A selective Review

Psychotic episodes are archetypes of severe psychiatric syndromes and of a profound disruption of psychosocial development with great personal strain and social and economical burden. More significantly, they mark the beginning of severe psychiatric conditions such as schizophrenia, bipolar and depressive disorders. Despite numerous advances in treatment of these disorders, morbidity and mortality and overall burden are one of the greatest in clinical medicine (reference on burden (C. J. L. Murray 1996; Rössler et al. 2005). The rise of "high-risk states" pinpoints such measurable risk and has allowed primary prevention (along such early detection and intervention) before the onset of a mature syndrome. This is a novel approach to severe mental disorders which attempts to change their natural history. Research has shown that such is a "uniquely evidence-informed, evidence-building and cost-effective reform provides a blueprint and launch pad to radically change the wider landscape of mental health care and dissolve many of the barriers that have constrained progress for so long" (McGorry 2015). This development has allowed nosological and phenomenological enquires in High-Risk states, has highlighted a range of categories and phenomena these patients go through and has allowed the trial of assorted preventive interventions.

There are various seminal inputs for the possibility of early symptoms of mental disorders as Griesinger and Kraepelin respectively "observation shows that most mental disorders are first manifested, not by senseless talk or extravagant acts, but by morbid changes of mood and anomalies of the self. The earliest stages of insanity consist of an "aimless feeling of ill humor (objectlosen Gefiihle der Unaufgelegtheit), discomfort, oppression, and anxiety…" (Griesinger 1867) "the beginning of a mental disorder is generally slow… only rarely it arises suddenly and is not preceded by a symptom. Notably, small changes along weeks or even years are the first and only evidence of an impending mental disorder" (Kraepelin & Lange 1927). In the case of schizophrenia there are various other authors focusing on early symptoms such as Bumke "the beginning of schizophrenic process is preceded by encumbrance, continuous headaches, fatigability and disquiet sleep. Occasionally they experience the loss of appetite, palpitations, anguish or vertigo. Other times ananchastic and incapacity to reach a decision (…) and hypochondriac complaints (…) patients can feel changed and unable to think adequately" (Bumke 1936). Notably, seminal literature on Psychosis has also focused in the actual pre-delusional state of mind, evoking good representations of what today would characterize a prodromal state ("the augury of something or happening" (Fava et al. 2008)). Important depictions include those of Jaspers ideas (Jaspers 1963) and of Conrad (Conrad 1958)). For instance, Conrad depiction the initial phase of psychosis "trema" was an invasive atmosphere with unaltered perceptions and yet an all-together perceptual field imbued with subtle change of uncertainty and threat. In these phase they would experience an increased tension "as if there was something in the air" and a reduction of their capacity to act upon reality (they felt they could not move or decide as before) (Conrad 1997).

However, most empirical research is traced only to the 60s' both to European Psychiatry in Huber's concept of basic symptoms ((Schultze-Lutter, Ruhrmann, et al. 2012)) (see below) and to American-Australian Psychiatry gather up of data that, two decades later, would serve as basis for retrospective early detection studies ((Häfner, Riecher-Rössler, Hambrecht, et al. 1992) (Häfner, Riecher-Rössler, Maurer, et al. 1992) (Häfner et al. 1998)) proposing that 73% of all patients with psychosis had a 5-year's prodromal phase ((Häfner et al. 1998)). Basic Symptoms are subjective disturbances in drive, affect, thinking, speech, perception, motor action, central vegetative functions and stress tolerance occurring in psychosis. For example, the basic symptom "Thought pressure", a self-reported ''chaos'' of unrelated thoughts, can be described as follows: ''If I am stressed out my mind gets chaotic and I have

great problems thinking straight. Too many thoughts come up at once.'' Unlike positive psychotic symptoms, basic symptoms are not associated with abnormal thought content and reality testing and insight is preserved (Gross 1989; Huber & Gross 1989). Longitudinal studies on basic symptoms in putatively prodromal patients by Klosterkotter (Klosterkötter et al. 2001) supported their very high sensitivity (96%) and high specificity (70%) for transition to schizophrenia.

In the 1990's in Australia, the criteria for a Ultra-High-Risk group were developed by Jackson and Mcgorry (Jackson et al. 1994) and the first clinical service for subjects at risk for developing psychosis was created by Yung et al (Yung et al. 1996). UHR criteria includes three cohorts of persons as high-risk: the attenuated psychotic symptoms (APS) group, including subjects with subthreshold (for intensity of frequency) psychotic symptoms; the brief limited intermittent psychotic episode (BLIP) which refers to phenomena that are frankly psychotic, but occurring for short periods of time; genetic risk and deterioration syndrome [GRD]) group which expresses vulnerability defined through family history of psychosis or diagnosis of schizotypal personality disorder in the individual couple with and decline in functioning.

Important conceptual clarifications include the distinction between initial, precursor, prodromal and basic symptoms all of which are used in this field. The concept of early symptoms is credited to Bleuler 1955 when portraying early schizophrenia (Bleuler 1950). They characterize pre-delusional states as including unspecific and seldom recognizable (1) affective symptoms, such as indifference and apathy, (2) obsessive and compulsive ideation and (3) "hysteric and neurasthenic" fluctuant symptoms. Prodromal symptoms are attributed to Mayer-Gross (Mayer-Gross 1932) and include change in activity, psychasthenic complaints and the lack of affective resonance, depersonalization phenomena, compulsive symptoms without anxiety, hypochondriac symptoms, compulsive symptoms, whirlwind thought processes (manic tonality). Huber and Gabriela Gross by analysing 757 cases of schizophrenia depicted precursor and prodromal symptoms (Huber 1985; Gross & Huber 1985; Huber & Gross 1989; Gross et al. 1987). While "precursor" symptoms preceded (months) prodromal phase and psychosis being of limited duration – hours/days (rarely months/years) the prodromal symptoms preceded but would continue on during psychosis having a fluctuating course. The concept of basic symptoms was laid by Huber (Huber & Gross 1989) to describe the subjective experiences lived and depicted by patients in the

initial phases of schizophrenia and in post-psychotic states. These included fluctuant cognitive, motivational (fatigability, reduction of energy and resistance, reduction in activity, indecision / ambivalence) and emotional experiences and the reduction in coping capacity (to changes), the will to be with others and patience (experience of irritability and discomfort). They also included perceptual disturbances ranging from sight, noise, taste and smell or cenesthetic experiences. These symptoms were not specific to schizophrenia but present in organic brain syndromes and in melancholic depression. However, a subset of basic symptoms has been found to be predictive of subsequent development of psychosis, particularly schizophrenia. These include nine cognitive disturbances (COGDIS), such as subjective disturbances of thought process (interference, blockages, pressure), as well as inability to divide attention, disturbances of expressive and receptive speech, unstable ideas of reference and captivation of attention by details of visual field.

Also it seems important to understand that criteria have aimed to select distinct features and that there are two different stances to understand the High-risk states. Interestingly they are akin to the bleulerian and schneiderian approach to Psychosis: while the first aims to select the "most fundamental symptoms" (BS) the second searches for "most frequent symptoms" (UHR criteria). UHR and BS segregate different and complementary cohorts of HR subjects, some saying even that BS aim to identify earlier prodromal phases and UHR to detect later and clinically more relevant phases (Keshavan et al. 2011; Klosterkötter et al. 2013). Some have suggested that their simultaneous use would allow higher significance for transition (Fusar-Poli, Borgwardt, et al. 2008). We'll quickly address the complexity and range of the categories used to identify the risk-of-psychosis as it seemed to us a first problem in the depiction of their core phenomena.

A simple approach is to assemble the objective symptoms used in the measures and instruments used in the depiction of these disorders. The UHR states are selected by a range of instruments that include the Comprehensive Assessment of At-Risk Mental State (CAARMS); the Structured Interview for Prodromal Symptoms (SIPS) and the companion Scale of Prodromal Symptoms [SOPS]); the Early Recognition Inventory for the Retrospective Assessment of the Onset of Schizophrenia (ERIraos); the Basel Screening Instrument for Psychosis (BSIP) or even a self-rating prodromal scale (Loewy et al. 2005). The CAARMS (created in Melbourne in the Personal Assessment and Crisis Evaluation (Yung et al. 2005)) and the SIPS/SOPS (developed by Miller et al (Miller et al. 2003)) are

Australia and America's respective equivalents, though both now also being used in Europe. The ERIraos assesses schizophrenia onset retrospectively and was created by Hafner et al ((Häfner et al. 2013)), and it is used in some German and Italian studies. The BSIP was developed in the Early Detection of Psychosis Clinic in Basel by Riecher-Rossler et al. ((Riecher-Rössler et al. 2007; Riecher-Rössler et al. 2008)). For the basic symptoms a comprehensive scale has originally been developed: the Bonn Scale for the Assessment of Basic Symptoms (BSABS) (Gross et al. 1987). In recent years, a subset of Basic Symptoms has been found to be specific to psychosis and associated with transition to psychosis. These cognitive and perceptual experiential features can be assessed by the Schizophrenia Proneness Instrument, Adult version SPI-A (Schultze-Lutter, Addington, et al. 2007) and child and youth version SPI-CY (Schultze-Lutter, Marshall, et al. 2012). Other instruments have focused in particular subsets of experiences including self-experiences as the EASE (Examination of Anomalous Self-experiences) and bodily experiences as the ABP (Abnormal Bodily Phenomena, developed by Giovanni Stanghellini). UHR criteria have now a comprehensive volume of research to sustain their clinical relevance and its consistency and validity ((Yung et al. 2006) (Carr et al. 2000) (Ruhrmann et al. 2010) (Broome et al. 2005)). These include (1) evidences from neurocognitive studies (for metanalysis see (Fusar-Poli, Deste, et al. 2012; Woodberry et al. 2008; J Giuliano et al. 2012) (2) genetic and imaging studies (for metanalysis see: (Smieskova et al. 2010; Fusar-Poli, Radua, et al. 2012; Fusar-Poli et al. 2011), functional (Fusar-Poli et al. 2007) and (3) neurochemical imaging studies (Fusar-Poli & Meyer-Lindenberg 2013b) (Howes et al. 2007; Stone 2009; Fusar-Poli & Meyer-Lindenberg 2013a).

A conceptual analysis of HR shows a significant heterogeneity by the fact that these states are considered with different epistemic (e.g. having a family history of schizophrenia) and phenomenic (e.g. Basic Symptoms and UHR symptoms) (Olsen & Rosenbaum 2006) grounds for diagnosis. This chapter focuses in attempting a phenomenological clarification of the criteria of UHR and BS. In the former, we focus mainly in the Attenuated Psychotic Symptoms group, which constitutes the sub-threshold experiences of a "psychosis at risk syndrome". It the latter we portray the development of the subtle alteration of conscious experience described by basic symptoms. Exploring the objective and subjective phenomena that these subjects undergo is key to segregate them from general anxious, depressive and depersonalization/derealization experiences.

An interesting account of UHR and BS is the attempt to further clarify, as in the First Episode of Psychosis, if the subject is at risk of schizophrenia. Indeed various sources of these criteria are from schizophrenia (including language disturbances, isolation and blunting of affect). Despite the fact that UHR criteria were originally meant to identify risk for psychosis broadly, research has shown that they are strongly biased towards detection of schizophrenic psychosis. A meta-analysis on 23 studies on subjects at risk for psychosis has shown that criteria for psychosis risk are biased towards an identification of early phases of schizophrenia spectrum rather than affective psychosis: 73% of subjects who transitioned to psychosis met schizophrenic spectrum criteria, while only 11% met criteria for affective psychosis.

Recent interest in studying the Bipolar at-risk state has allowed new instruments being developed to select subjects at risk such as the Bipolar Prodrome Symptom Interview and Scale–Prospective (BPSS-P) (Correll et al. 2014). However, these are not currently routinely included in UHR assessment.

2.1 Attenuated Psychotic Symptoms and Basic Symptoms

This section assembles and details the phenomena that have been considered both in the APS and BS as providing early detection of risk of developing psychosis. Despite the amount of research on the presence and reliability of these symptoms we recommend some phenomenological apriori premises that should be borne in mind when analysing the available literature. First, many of the phenomena that are studied in the HR are transposed from full-blown functional psychosis (particularly schizophrenic psychosis) and were therefore depicted in psychiatric disorders and not in adolescence or early adulthood. The narration of these experiences in schizophrenic and affective psychosis involves the coexistent thought and perceptual disturbances that might include changes in the psychopathological symbols being used. This leads us to the second suggestion – that the "intact insight and reality testing" considered in the HR states is key the psychopathological import of derealization and depersonalization experiences. The derealization and depersonalization that are deeply imbued in the construct of psychosis rely highly in the fact that the person has loss contact with reality as other forms of these experiences are fairly common in non-psychotic situations such as in anxiety and adaptive reactions (e.g. delusions and hallucinations). So for them to remain valuable in the assessment of High-risk states

great care and detail should be taken in the analysis of the phenomena these persons portray. And this hints at the last problem: that the concept of psychosis stands for a radical change in subjectivity which includes a loss of contact with reality and a heterogeneous range of phenomena where thought processes, new bodily and world meanings occur and lead to subjective arousal. The phenomena in HR states, by their inceptive nature, are conceptually apart from the drastic change of a psychotic state. All three reasons make the phenomenological enquiry of these states as stimulating as ambitious and we present the state-of-the-art of their study across objective and subjective phenomena.

2.2 Objective phenomena of HR

The identification of the objective phenomena occurring in HR states can come from the psychiatrist but also by family and friends who identify various behavioral changes which are present in a third person perspective. Most of them involve changes in social and occupational functioning. Some of these symptoms are identified as negative symptoms including being socially withdrawn and presenting autistic features. In addition to (and often preceding) attenuated positive symptoms of psychosis, social isolation, impaired occupational functioning and difficulties in interpersonal relationship, as well as other negative symptoms, are among the main presenting complaints of subjects seeking help and meeting criteria for psychosis risk. In fact, impairment in psychosocial functioning is a characteristic feature of the psychosis risk state (Velthorst et al. 2010), associated with poor longitudinal outcome (Fusar-Poli et al. 2010).

Moreover, HR subjects usually present with comorbid diagnoses, such as anxiety, depression, and substance use disorders ((Fusar-Poli, Nelson, et al. 2014) (Lencz et al. 2004; Fusar-Poli et al. 2013). Multicenter studies on large HR sampled showed that the most common positive symptoms are unusual thought content and perceptual abnormalities. Regarding negative symptoms, half of HR subjects endorse poor functioning and a significant proportion presents decreased ideational richness, while disorganization symptoms are less frequently noted. ((Addington et al. 2015). Trouble with focus and attention is usually the most common disorganized symptom, whereas dysphoric mood is the general symptom endorsed more often (Alderman et al. 2015). Some studies reported more severe negative symptoms at presentation, followed by positive, general and disorganization symptoms (Ruhrmann et al. 2010; Comparelli et al. 2014; D. Fulford et al.

2014; Lee et al. 2014; Velthorst et al. 2009). Amongst negative symptoms, social anhedonia is the most common. Suicidal ideation is also present in a significant proportion of patients at risk for psychosis. More than half of HR patients has at least mild suicidal ideation, while almost half of them have attempted suicide before engaging with an Early Intervention Service (Hutton et al. 2011).

2.3 Why are Self Disorders linked with High-Risk of Psychosis?

Many, if not the larger part, of the phenomena that constitute APS and "basic symptoms" are self-reported and subjective in nature. Some are broad-spectrum and encompassed in descriptive psychopathology textbooks including neurotic-like symptoms as changes in concentration and attention, reduction of initiative and motivation, general anxious and depressive moods and social isolation. This section else focus in subjective phenomena specifically referred to these states in accordance to the seminal contributions (see before) and to recent reviews (Yung & McGorry 1996; Klosterkötter et al. 2013). Part of it purposely overlaps with that of previous sections – aiming to reiterate the relevance of self disturbances as HR factors. Moreover, it details Abnormal bodily Experiences and Truman Symptoms as means to operationalize the subjective life of HR subjects.

2.3.1 Disturbed grip on reality: perplexity, derealization and depersonalization phenomena

Early psychiatric literature portrays the features of impending psychosis as arrangements of perplexity, depersonalization and derealisation experiences which are included in the ideas of delusional atmosphere/mood ((Jaspers 1963) (Schneider 1959) (Binswanger 1957) (Conrad 2013) (Matussek 1952). Such states are depicted as a "psychologically irreducible...subtle, pervasive, and strangely uncertain light" - intolerable but vague content (sensations, mood)" (Jaspers 1963) and "Sinister and disquieting experience that perceptions mean something which is vague but menacing" (Schneider 1959). The perplexed subject is depicted as enduring 'the oppressive awareness of one's inability to cope with a given internal and external situation, this awareness being experienced as something that cannot be explained, something that has to do with one's own self' (Störring 1987) (Storring 1940). This subject also undergoes a decrease in the empathic capacity and/or a decline in psychic and motor activity and/or a detachment from the world (perception) (Störring 1987). The

relation of perplexity with early psychosis is inscribed in seminal contributions as in (1) Conrad's depiction of *trema* described as a state of hyper-awareness similar to what an actor experiences just before entering the stage where reality is saturated with hidden/mysterious qualities that strike the subject with an uncanny salience (Conrad 2013) and (2) to subjects portrayal of being "at-mercy"(ness) as if "hooked to the perceptual elements" (Blankenburg in (Jenner & De Koning n.d.)) or (3) of being enslaved to the world they perceive (Matussek P: Studies in delusional perception (translated and condensed in (Cutting 1987))).

At an abstract level, HR subjects are said to endure a primary form of disturbed "grip" or "hold" on the world (Sass & Parnas 2003; Borda & Sass 2015) which involve deficits (1) in context processing and (2) abnormal discrimination between familiar and strange stimuli leading to perceptual disorganization and disintegration ((Martin & Pacherie 2013; Sass 2004)). A composite loss of "Perceptual organization" establishes a failure to structure stimuli ((Uhlhaas & Silverstein 2005) and of "Perceptual Integration" constitutes a disturbance of intermodal synthesis (Postmes et al. 2014). These have been found in schizophrenia samples and ground various deficits in these subjects ((Uhlhaas & Silverstein 2005; Phillips & Silverstein 2003; Postmes et al. 2014)). The HR subject is hypothesized losing the ability evaluate of context particularly differentiate external and internal stimuli which together constitute their unstable reality (that lacks clarity) and their disturbed feeling of *presence* ((Nelson, Whitford, Lavoie & Sass 2014b; Nelson, Whitford, Lavoie & Sass 2014a) and below).

These subjects also endure another form of disturbance of "grip" conceptualized as the incapacity to coherently deal with the foreground stimuli. Such impediment leads to a disturbed focus and to a rigid attention where relevant and non-relevant stimuli both become salient. This was coined "the abnormal salience hypothesis" {Kapur:2003dl} depicting how stimuli usually in the background come forward and interfere with those of the foreground. It constitutes a form of disturbance of attention where the subject is unable to focus or becomes abnormally focused on specific stimuli (Fletcher & Frith 2008) (Kapur et al. 2005) (Kapur 2014) (Nelson, Whitford, Lavoie & Sass 2014a) (Matussek 1987) (Postmes et al. 2014). Such changes occur early on in HR states where the subject complains of losing his ability to focus and his affordances (Gibson 2014) – meaning the things that were previously important in the subjects experiential world. The HR subject finds it difficult to navigate in

a world deprived of personal meanings (Sass & Pienkos 2015) and moreover easily forms strange perspectives on the world (Sass & Byrom 2015) he inhabits.

Some reservations do however remain regarding the use of such "disturbed grip" (and consequential depersonalization and derealization) as a marker of the risk of psychosis. They stand on these experiences being phenomenological complex (Simeon et al. 2008), (Simeon & Abugel 2008) allowing for different forms. Moreover, depersonalization/derealization are also the third most common psychopathological symptom (after anxiety and depressive mood) occurring in non-schizophrenic pathologies, in normal adaptive reactions to anxiety-provoking situations or even as voluntary responses (e.g., in introspection or meditation (Sass, Pienkos & Nelson 2013)). It would then be possible that anxiety disorders, depressive disorders (Brauer et al. 1970) and Depersonalization Disorder (Simeon et al. 1997)) could have their own constitutive forms. Indeed, attempts to break through this phenomenological complexity could be helpful in this distinction (Simeon et al. 2008). A simplistic appraisal postulates particular forms as (1) a "melancholiform" form depersonalization constituting a *state* of reduced vitality where sensations or emotions are less vivid and (2) a "schizophreniform" form of depersonalization that would be *traitlike* internal distance one self which becomes externally observed (one's own body, mind, thoughts, emotions, actions), reflected upon (hyper-reflexivity) and therefore felt with a sensation of alienation.

Yet it is also possible to conceive that for the latter forms (considered of schizophrenic bearing) there could be *secondary* forms ((Sass 2014) (Borda & Sass 2015; Sass & Borda 2015) (Hunt 1976), (Sass, Pienkos & Nelson 2013; Sass, Pienkos, Nelson, et al. 2013)). At an epistemic level, these secondary or consequential forms would arise as defensive factors that occur *in* but are not distinctive *of* schizophrenia. Phenomenologically they would be akin to the primary forms yet they would occur in the above disorders even have volitional (or quasi-volitional) counterparts would take place in introspection or meditation. Indeed, and beyond this theoretical consideration, recent studies (Sass, Pienkos, Nelson, et al. 2013; Sass, Pienkos & Nelson 2013)) have explored specific *patterns* that would in term allow the clarification of schizophreniform, non-schizophrenic forms (Sass, Pienkos, Nelson, et al. 2013) or even non-pathological forms (Sass, Pienkos & Nelson 2013) of these disturbances.

These disturbances in understanding reality are intimately related with three other experiences in HR states that are detailed next – an increased preoccupation and cognitive

introspection (hyper-reflexivity), a change in the feeling of "presence" and the experience of singularity of existence.

2.3.2 Hyper-reflexivity: (in) voluntary rumination and inward attitudinal stance

This refers to the complaint of an increasing tendency (volitional and non-volitional) to attend to internal processes and to phenomena which were previously tacitly dealt to which the subject was not self-conscious (Sass 1992; Sass et al. 2011). The first (and rather obvious) explanation for HR subjects' self-absorption derives from the alienation that their states involve – solitude as ground for thinking. Yet, and hinting a possible primary involvement in HR states, is that similar self-absorbed configuration of experience is a primary feature of Conrad's depiction of delusion formation – "the subject turns inward, reflecting and introspecting upon the most trivial things" (Conrad 2013). Further detail into the latter arrangement has conceptualized this as a psychopathological symptom with two forms – primary (operative) and secondary (compensatory) – a division which appear to be supported by the latest translational studies.

Automatic or "Operative Hyper-reflexivity" is related with the previously portrayed "salience hypothesis" (Kapur 2014) (Roiser et al. 2013) – elements previously in the background of the perceptual field become salient and in need of reflection. The subject sense of self is disturbed as such – the normal sense of self – requires that consciousness is at least partially turned *off*. Such form of "*overthinking*" is intimately linked with the feeling of being a spectator of one's experiences – no longer *living* (being in the world) and rather *thinking* (musing on the world). Sass provides an interesting account of such as a "subtle but pervasive replacement of natural engagement in the world with introspective ruminations" (Sass et al. 2011). Such is conceived as resulting from a disturbed perceptual intermodal integration and also, and particularly, the inability to "triangulate" all sensory inputs (afferent/body ownership) from his self-in-action (efferent/body agency) (Gamma et al. 2014; Jeannerod 2003; Parnas et al. 1996; Schwabe & Blanke 2007; Tsakiris et al. 2007; Tsakiris 2010; van den Bos & Jeannerod 2002; Wylie & Tregellas 2010).

Reflective (or secondary) hyperreflexivity refers to ancillary form of overthinking – aiming attention to what would normally be experienced as part of oneself or yet – moving focus from the explicit world to the implicit dimensions of experience (these include cenesthetic

and proprioceptive experiences). Seminally, this subordinate upsurge in cognitive rumination was conceptualized by Blankenburg (Blankenburg 1971) as a consequence of Verlust der natürlichen Selbstverständlichkeit (loss of the natural self-evidential nature of anything). Such loss of natural evidence is another link between forms of hyper-reflexivity and previously depicted disturbed grip on reality and the feeling of perplexity that imbues HR states. Neurobiologically such could constitute the (over) activation of Default-Mode Network involved in "self-referential" tasks (Nelson, Whitford, Lavoie & Sass 2014b) (R. J. Murray et al. 2012) (Northoff et al. 2006) (Qin & Northoff 2011) (van der Meer et al. 2010), part of the "neural circuitry of self (Brent et al. 2014) and an altered salience of perceptions (Nelson, Whitford, Lavoie & Sass 2014a)

This is closely related with the reduction in the feeling of being present in the world (next section) as in all three forms of hyper-reflexivity (isolation, primary and secondary) as "thoughts" are experienced unsuitable alternatives to previous experiential features and understanding of the world – and a painful distance to the world takes hold.

2.3.3 Diminished self presence: experiential distance

Another key feature of High-risk states is the sense of decline in one's presence in the world together with the feeling that experience is no longer unique to the subject (Sass & Parnas 2003) – shorn of its Meinhaftigkeit or moiété [myness] and could now become of everyone else. Again as with hyper-reflexivity, the loss of self-presence is conceptualized as both primary and secondary. Primary diminished Self Presence (diminished self-affection) refers to the loss of being present as living and being a unified subject of awareness or agent of action. It is an expression of the distortions of first-person perspective resulting from the loss of ipseity, which would be discussed in a subsequent section of this chapter. At first it can be seen in close relation with the previous experiences (1) the subject can no longer take for granted his selfhood and (2) many tacit experiences become salient and explicit. Yet such reduction involves more than the loss of ownership and agency to entail also the failure to distinguish oneself from others ((Herrera et al. 2006; Lallart et al. 2009; Riva et al. 2014; Zahorik & Jenison 1998)). Neurobiological evidences for disturbance of body ownership point to disturbance of bottom-up multisensory integration and areas such as right temporo-parietal junction (TPJ) and posterior parietal cortex ((Ehrsson et al. 2005; Tsakiris et al.

2008)). These areas together with the somatosensory cortex and the insula are responsible for the neuronal representations of a bodily self (see more in (Borda & Sass 2015)).

Else another form – here devised secondary – of diminished self-presence refers to the intentional or defensive process of withdrawing from the world and reducing the sense of existing or of being an agent of action. Many of the previous experiences involve variable degrees (usually high) stress levels that together with the persistence of a sense of not being able to cope with reality result in an appalling experience. It would not be surprising if the HR subject attempts to remove himself from such reality and to increasingly aim for self-objectification (increase clarity on his reality). Indeed such could also explain some of the depersonalization phenomena occurring in post-trauma which would motivate such secondary form of removal. These processes appear to involve the same brain correlates – hyperactivation of the Default-Mode Network (DMN) and the hypoactivation of Central Executive Network (CEN) of the salience network (Moran et al. 2013) (Nekovarova et al. 2014) (Nygård et al. 2012) (Sass & Borda 2015).

2.3.4 Eccentric/ stance and existence as "singular"

Another subjective phenomenon occurring in High-Risk states is the fact that narratives of life laws and events involve a sort of peculiarity – accounts of reality are singular/exceptional and their option for eccentric stances on the world (antagonomia) (see more in (Stanghellini & Ballerini 2007) and (Parnas, Møller, et al. 2005)). These include phenomenological diverse experiences that range from transformations personal narrative or solipsistic beliefs on the world to concrete/tangible changes in the way that the world is perceived. The former refers to the disturbance of autobiographical *continuity* and a feeling of *singularity* in one's existence in the world – composite forms resulting from the subject "being struck" new meanings in his everyday life. The first refers to not having a coherent narrative as if the "rules of one's life" and "nature of one's events" were frequently anew and in need of reintegration. The idea of singularity of reality is related to the previously depicted disturbance of salience or in Sass words – "everything is strange, or everything is somehow different" designated by "uncanny particularity" (Sass 1992). Everyday routines and perceptions that were fortuitous and to which the subject was oblivious and detached become striking. In High-risk states it differs from such everyday experiences becoming salient to subject which endures a striking uniqueness of events – as if something extraordinarily

private (evading understanding) was now entailed in the objects in the perceptual field – "I had to stop by that tree. True, it had always stood in front of his house but an utter amazement of its uniqueness made me stand by to appreciate why was the tree here?" Every experience is fresh and reality elements present themselves as if they were new.

It should not be understated that all these occurrences are under the umbrella of the disturbance of ipseity. These abnormalities unremittingly grind the patient's links with reality. Together they provide the patient with numerous stimuli to process simultaneously, promoting his attention to inward stimuli and undermining the "common sense". If these phenomena progress, the patient further experience states of solitude hindering his responsiveness to real requests from the external world. Such further disrupts the already disturbed core sense of personhood, segregating the patient from reality and making him lose contact with that same reality. When this happen, those non-yet psychotic abnormalities of the experience of the self, previously characterized by an "as if" characteristic, evolve into fully blown psychotic symptoms.

2.4 Special Sets of Phenomena

The following phenomena are selective sets that group the previous phenomena into meaningful clusters of symptoms. Their standard in HR research appealed to us the needing the special detail below.

2.4.1 Truman Symptoms

One of the special forms of derealization and perplexity recognized in High-risk states (Madeira, Bonoldi, Rocchetti, Brandizzi, et al. 2016) was symbolized into the construct – "Truman symptoms" (TS) (Fusar-Poli, Howes, et al. 2008). The idea refers to 1998 Peter Weir's movie, in which the protagonist (Truman) is first unaware of being in a television show and gradually becomes suspicious of his world being constructed reality (Fusar-Poli, Howes, et al. 2008). TS represent a profound change of the subjective experience and of self-awareness, resulting in an unstable first-person perspective with varieties of derealization, disturbed sense of ownership, fluidity of the basic sense of identity, distortions of the stream of consciousness and experiences of disembodiment (Fusar-Poli, Howes, et al. 2008). They involve rumination on altered subjective phenomena and an increasing self-

awareness Keeping the “as if” component (not a delusion), he might reach a “Truman explanation” that explains what, how and why he experiences that.

TS are particularly relevant to the psychopathology of UHR group as a form attenuated psychotic symptom (Fusar-Poli, Howes, et al. 2008) and because they apprise the cultural expression of a psychopathological phenomena in a group familiar with the information technologies (such as the internet and virtual reality).

2.4.2 Anomalous subjective Self-Experiences

The disturbances of the self (Sass 1992) (Kircher & David 2003) (Parnas et al. 1998) (Sass & Parnas 2003) (Zahavi 1999) contain the many of the previous portraitures on subjective symptoms and are today central topics of psychopathological research in High-Risk subjects (Brent et al. 2014) (Nelson et al. 2008) (Nelson et al. 2012; Nelson, A. Thompson & Yung 2013) (Stanghellini et al. 2013). For disturbances of the “basic” / “core” / “minimal” self are considered the primary disturbance – mainly representing a disruption of ipseity. Such loss of ipseity would then forefront the distortions of first-person perspective (diminished self-presence and self-affection, the changes in process of thought and perception (disturbed grip on the cognitive-perceptual world) including the loss of “natural evidence” and increased reflexivity and also derealization and depersonalization experiences (see above). Disturbances of basic-self have strong neurobiological translational research (Borda & Sass 2015) (Sass & Borda 2015) accounts of delusion formation in prodromal and early phases of psychosis that point to a neurobiological underlying alteration in salience processing of stimulus

(Mishara & Fusar-Poli 2013; Roiser et al. 2013; Winton-Brown et al. 2014). The range of the experiences resulting from the disturbance of ipseity have been operationalized in the EASE interview – Examination of Anomalous Self-Experiences. This interview selects phenomena which involve “subjectively experiencing” a (1) disturbed way of thinking, (2) being in the world, (3) one’s own body, (3) interpersonal relations and (5) principles and attitudes on the world one lives in. Also it has shown a good internal and external validity and its use in subjects in high-risk of psychosis (Nelson et al. 2012; Nelson, A. Thompson, Chanen, et al. 2013; Nelson et al. 2009; Nelson, A. Thompson & Yung 2013) and in prodromal phases of schizophrenia (Parnas 2005; Nelson et al. 2012) has suggested they

could be used as an early marker. It should not be understated that a crucial feature of this model is the fact that it is should be assumed as an "overall," "holistic," or "gestalt-like" disturbance and not as indexed to a single (quantitative) measure ((Parnas, Moller, et al. 2005) (Parnas et al. 2014)).

2.4.3 Abnormal Bodily Phenomena

A similar research track has now explored the prevalence and relevance of ABP in patients with first psychotic episode and, in particular, in subjects with diagnosis of schizophrenia (Stanghellini et al. 2012; Stanghellini, Ballerini, Blasi, et al. 2014)2.

Abnormal bodily phenomena (ABP) have been considered in patients with psychosis and particularly schizophrenia even in their seminal representations (Jaspers 1963). The notion of ABP is related with the ideas of disturbed coenesthesia (Röhricht & Priebe 2002), assortments of uncanny bodily feelings with or without delusional interpretation, kinesthetic hallucinations (Ey 1973; Uhlhaas & Mishara 2007) and disruptions of body structure and boundaries (see more in (Stanghellini, Ballerini & Cutting 2014)). As a group, ABP are subjective phenomena that were taken as quasi-ineffable in nature and lacking sensible, specific and reliable tools to assess them and therefore, until recently, absent from our diagnostic textbooks.

The "Abnormal Bodily Phenomena Questionnaire" (ABPq) (Stanghellini, Ballerini & Cutting 2014; Stanghellini et al. 2012) allows a systematized enquiry of these experiences. Studies using ABPq have shown an assortment of bodily phenomena occurring in schizophrenia (Stanghellini, Ballerini, Blasi, et al. 2014) and the in the first episode psychosis(Stanghellini et al. 2012). These include uncanny feelings of numbness, loss of body vitality, the sense of disappearance of parts, change in form (as shrinking or enlargement), dimension (as unusual heaviness or lightness) or even "movement of internal parts" of the body (Stanghellini, Ballerini, Blasi, et al. 2014; Ey 1973; Dupré 1925). Examples of these phenomena are presented in the ascribed textbox.

Various studies suggest that ABP occur as trait features before the first psychotic episode in patients with schizophrenia (Hemsley 1998; Klosterkötter et al. 2001; Röhricht & Priebe 2002; Stanghellini 2009b; Gallese & Ferri 2013; Schultze-Lutter, Ruhrmann, et al. 2007).

The Comprehensive Assessment of At-Risk Mental State scale (reference CAARMS) already selects disturbances of bodily phenomena as relevant to the HR profile. A recent study (Madeira, Bonoldi, Rocchetti, Samson, et al. 2016) explored the prevalence and implications of Abnormal Bodily Phenomena in subjects considered at high risk of psychosis and found they were highly prevalent (while absent from matched HC) raising the possibility that ABP could be a phenotypic component of HR psychopathology. Some of the assorted ABP experiences reported by the HR subjects included: the experience of violation "when he stretched his hand I felt an energy entering my body. That energy was pounding my right side until it break in"; experience of externalization "I felt that my body had become as a boiling soup and I was no longer in control of my energy that flows around me. Then my body became an ingredient in the soup parts of me are the vapors and rest of the soup"; morbid objectivization "I felt my brain freezing. Then thoughts were moving so slowly I could feel them drive from ear to ear" and devitalization "The loss of the animal part in me, I lost it! I feel that I act as I was programmed, even eating and I feel like a robot, even my arms feel artificially attached to me" (among others, see (Madeira, Bonoldi, Rocchetti, Samson, et al. 2016)).

2.5 Why are HR relevant to contemporary research in Psychopathology?

The relevance of this contemporary field of research comprises ontological (considering the possibility of prevention and early intervention in psychiatry) and epistemological (merging of assorted neurobiological, philosophical and epidemiological contributions) novelties. To handle and keep expanding such breadth of knowledge, researchers and clinicians should bear enough conceptual and phenomenological knowledge on the experiences that occur in High-Risk sates. Such knowledge is vital in contemporary predictive and translational research which will ultimately guide the integration of phenomenological data with the neurocognitive and neurobiological models (do you like this as it is Ilaria?). This chapter reviewed the assortment of phenomena portrayed by subjects in HR states of Psychosis and focusing in subjective symptoms. In this sense, HR states not only bear the anticipation of a new scenario in the identification and treatment of psychiatry disorders but also they have been, and must continue on being, an archetype of a phenomenologically-informed psychopathology.

4. The state of the art of dissociation

The nature of the distress of depersonalization experiences displays the complexity of human subjective experience suggesting the possibility of suffering not only through the presence of a feeling but also by the lack of feelings. Derealization implies that the meaning of experiences is not immediate but a process inner attribution of meaning (and conceptualization) in which if disturbed can lead to different amounts of perplexity (or even loss of natural evidence). Most of the descriptions are made by metaphors adding to the overall idea that these changes in engagement with the world, enactment of meanings and periods of loss of awareness are not easily transmittable. As a group, DP are complex as they involve (1) a large range of phenomena and (2) they occur in a large number of psychiatric and neurologic disorders as well as in healthy persons. The idea of dissociation in psychiatry has had various inputs and such is expressed in symptomatology (conceptual halo) and nosology, as in the different stances about dissociative disorders expressed in DSM-5 and ICD-10 (Association 2013) (World Health Organization 1992). As with other psychiatric symptoms, DP are in need of increased conceptual and phenomenological examination. Dissociative disorders as a broad category raise criticism on the "lack (of) a single, coherent referent ... that all investigators in the field embrace" (chapter by Cardena in (Lynn & Rhue 1994)) and yet some of its central categories have shown phenomenological consistency (as is the case of depersonalization (Sierra & Berrios 2001)). Dissociative amnesia, depersonalization (and de-realization), conversion symptoms (somatic symptoms), pseudo-hallucinations, trance and self-disturbances are taken as classic dissociative phenomena.

The up-to-date manuals including the ICD-10 (Association 2013) (World Health Organization 1992) and the DSM-5 (Association 2013) use mainly an epistemology of changes of consciousness and the separation of “mental functions” (Hilgard 1973). The ICD-10 takes dissociative phenomena as a partial or total loss of (1) an integrated memory system, (2) a conscious awareness of identity or sensations and (3) the control of bodily movements and DSM-5 details it as a “separation of mental functions usually integrated and consciously accessible” comprising either/both memory, identity, perception, emotions and will (Hilgard 1973). The DSM-IV was reorganized in the DSM-5 to increase the homogeneity of the categories – depersonalization/derealization disorder instead of depersonalization and accepting dissociative amnesia as encompassing dissociative fugue. Overall the clinical use of both classifications involves intense criticism as patients are frequently assigned with the

diagnosis of “dissociative disorder not otherwise specified” ((Saxe et al. 1993) and Kihlstrom in (Lynn & Rhue 1994)).

An historical review of the conceptual models for dissociation is out of the scope of this chapter and can be found in a comprehensive review by Onno van der Hart and Martin Dorahy (Dell & O'Neil 2010). From their analysis some important ideas are retrieved. First the conceptualization of dissociation is riven from the very start as (1) a detachment of parts of personality in Puysegur, Moreau de Tthes, Gros Jean and Taine or (2) the occurrence of double consciousness described in Charcot, Feinkeind, Janet and Binet (see more in (Dell & O'Neil 2010)). The former suggests a disorganisation of the incorporation of personality elements. The latter proposes a behavitheal override by an independent mental structure that the subject is unaware and that burst directly as a response to a stimulus.

An important epistemological quarrel included dissociation being considered a phenomenon, a neurological explanation or a psychological understanding. As an explanation dissociation is seen as the mechanism of the conversion symptoms in Psychiatry and of functional symptoms in Neurology. The latter has provided dissociation another delicate aura – functional symptoms stand for absence of an organic explanation that neurologists would claim real (dissociation=absence of a real cause). As a psychological explanation (e.g. psychoanalytical inputs) dissociation stands as the most relevant conceptualization of hysterical symptoms by the separation of psychological elements under the light of preceding stressors (traumatic experiences). Further studies have suggested a consistent psychological and biological correlation between trauma and dissociative phenomena (see seminal work by Ferenczi (Putnam 1989). As a phenomenon, dissociation is also represented in the ideas of depersonalization, fugue state and dissociative amnesia. Dissociative phenomena as a group are troubling as each phenomenon occurs in contrasting situations (e.g. depersonalization in Anxiety Disorders and dissociative amnesia arising in patients that do not express clear anxiety symptoms and can sometimes show “la belle indifference”). Linking the previous considerations lead to even more intricate possibilities as depersonalization being considered a dissociative phenomenon with an anxious explanation (Baker et al. 2003; Sierra et al. 2012) or as a mechanism (detachment) of dissociative phenomena (Holmes et al. 2005).

Dissociative phenomena must also be distinguished if they occur (1) as a lifelong trait as in patients with schizoid, borderline and anxious personality disorders or (2) in particular states as in depressive episodes, panic attacks or epilepsy (C. Krüger & Mace 2010). Trait dissociation also appears to be phenomenologically related to the idea of schizophrenic autism and other basic symptoms. This discussion renders some troubles in the conceptualization of other dissociative phenomena as for instance amnesia in its anterograde form (inability to encode while in the situation) appears as a state while retrograde amnesia (inability to retrieve elements of past situations) might occur as trait.

Another input is that dissociative phenomena could also accept lighter deviations of consciousness (e.g. daydreaming) suggesting that it is dimensional with non-pathological states (e.g. meditation). This discussion is age-old and materialized in the seminal quarrelling by (1) Pierre Janet who supported that true dissociation only occurred in mental patients, specifically in hysteric subjects (Janet 2015) and (2) William James (James 1950) and Morton Prince (Prince 2015) who suggested it was dimensional occurring in adaptive and useful experiences (e.g. during stressful events) or in pathological situations. Some empirical studies support that a class of dissociation is pathological (Waller et al. 1996) and yet still with no nosological bearing as it occurs indistinctively in diverse taxonomical categories such as dissociation, schizophrenia or PTSD (Waller & Ross 1997).

4.1 Specific dissociative experiences

As discussed, by rule, dissociative experiences are the psychogenic counterparts of somatic and neurological symptoms and can possibly feign any physical or mental symptom – therefore all forms of human experiences (normal or disordered) can be considered dissociative. These would include flashbacks, identity confusion, psychotic-like symptoms, visual hallucinations (Steinberg et al. 1990) or even Schneider first rank symptoms (Ilhan Yargiç et al. 1998). Yet it is possible to separate experiences that are considered classic forms of dissociation (having a dissociative mechanism). This section reviews dissociative amnesia, depersonalization (and derealization), conversion symptoms (somatic symptoms), pseudohallucinations, trance and self-disturbances. They are not specific of dissociative disorders as they are present in several axis I (e.g. self disturbances in schizophrenia) and axis II categories (e.g. self disturbances in emotionally unstable personality disorder)

Amnesia

Dissociative amnesia has been clinically relevant since (ABELES 1935) and is the most common dissociative experience. It consists in trouble to retrieve or recall memory data including entire chapters of life from hthes to years (Leong et al. 2006). Traumatic events are often contemplated as the causative element and conventionally there is no brain lesion explaining such loss. It is discussed whether dissociative amnesia is a form of neurological memory disorder (Lucchelli & Spinnler 2002) as its neurological etiology (entertaining, for instance, a Transient Ischemic Attack) and relations with other disorders have been extensively reviewed (Serra et al. 2007). Recent research has changed the position of dissociative fugue so that it has become a specifier of dissociative amnesia (Association 2013). Fugue states involve behavior (many times unplanned travel or wandering) that is sometimes described by the subject or others as corresponding to a new personal identity and to which the subject will have no memory of. It is usually precipitated by a stressful episode (see details in DSM-5 2013).

Dissociative fugue, now under the topic of dissociative amnesia in the DSM-5, includes states, which there is wandering involved with behavior different from habitual self. There have been many theories regarding the etio-genicity of fugue states including organic disorders as cranial trauma (Berrington, 1956) and epilepsy (Broglin 1992).

Depersonalization

Despite of the statement of a relative stability on the core concept of depersonalization (Sierra & Berrios 2001), its phenomenology and epistemology has suffered interesting but not always compatible progresses. Differences in seminal descriptions already show-striking differences, as in Griesinger and in it's coining by Dugas in 1898 (see more (Sierra & Berrios 1997)). Griesinger's account suggests that it is "as if each of my senses, each one part of oneself was separated from me and couldn't offer me any feeling, my eyes see and my spirit has perception but the sensation of what I see is absent" (Griesinger 1867). He had proposed a change in self-affection and a reduction of patients' experience (also in portrayals by Esquirol and Billod). Dugas' else envisioned a loss of understanding and perplexity: "alienation of personality, a state where thoughts and acts become strange to the self". These conceptions anticipated many other elaborations: (1) a change in the sensorial modalities as

portrayed by, (2) disturbances in the potency of perception (Störring 1987); (3) a change in memory (Kraepelin & Lange 1927); (4) a change in Self-Experience (Janet in (Putnam 1989); (5) and a change in emotions, whether of, (6) a diminished feeling of activity or (7) of diminishing existential feelings (see more detail in (Sierra & Berrios 1997). Jaspers added that depersonalization could also be the awareness of alien and automatic perception, memories, ideas, thoughts and feelings (Jaspers 1963).

Somatic Symptoms

Many mental disorders are considered as having dissociative bodily symptoms (e.g. cenesthethic or pain experiences), frequently named conversion symptoms (in Psychiatry) or functional symptoms (in Neurology). Some hospitals have generated special units – Neuropsychiatric wards – that deal with these situations that frequently are non-responsive to psychopharmacological treatment.

Pseudo-hallucinations and true Hallucinations

Dissociative experiences occur sometimes as perceptual abnormalities that are often declared as pseudo-hallucinations for their odd phenomenology (e.g. hallucinations within one's head) and inconsistent clustering with other symptoms that are commonly together. Nevertheless, true auditory hallucinations were described in Dissociative Identity Disorder (DID) both in form of commenting and command voices (Dell & O'Neil 2010). Visual hallucinations occur though frequently need to be phenomenologically detailed for the differential diagnosis from flashbacks. Such peculiar perceptual changes are akin to the experiences described in the EASE for their psychotic-like status but yet remaining below the threshold of true psychotic experiences.

Trance

The experience of trance is considered beyond the limits of mental disorder (anthropological studies) and any psychiatric frame for such experiences need a cultural analysis. Trance states are different from fugue states as the subject experiences a change in his personal identity but remains fully aware of the surroundings(Dell & O'Neil 2010). Also most trance experiences are empowering or voluntary/semi-voluntary. The voluntary nature of trance is

akin to introspection and its relation discussed earlier in this chapter with basic-self experiences.

Self-disturbances

Though many times ignored the change in the sense of Self is the sixth most frequent dissociative symptom in DID and the psychophysiological processes that derive in dissociative experiences include a disturbance in the sense of self. These are the core experiences explored in the remaining chapters and therefore explained in much detail before.

5. Narratives and the limits in the accessibility to meanings

One of the topics in this thesis is that there is need of careful phenomenological exploration of patients narratives. It focuses in detailing the differences between "psychotic-like experiences" with no psychopathological bearing and those phenomena that could be risk factors / markers of a psychiatric disorder. Indeed, basic-self disturbances are expressed through the patients' narratives and reliant on that these narratives being good representatives of basic self phenomena. For there are two scopes which are significant to this essay: (1) a portion of patients identity seem linked to their ability to form and report narrative accounts of their life (McLean et al. 2007) and (2) psychiatric methods for diagnosis and research are dependent on *narratives* as means of systematizing experiences.

The first topic includes the way one finds a coherent self-narrative for his life and how that is a part of one's self-concept beyond all experiential and physical domain – "*the corporeal envelope of the friend had been so well stuffed with all this* (narrative details), *as well as with a few memories relating to his parents, that this particular Swann had become a complete and living being, and I have the impression of leaving one person to go to another distinct from him, when in my memory, I pass from the Swann I knew later with accuracy to that first Swann whom I rediscover the charming mistakes of my youth and who in fact resembles less the other Swann than he resembles the other people I knew at the time, as though it were the same in life as in a museum where all the portraits from one period have a family look about them, one tonality*" (Proust 2003). The author alludes to the idea narratives (both autobiographical and of others) are part of the identity one has both for himself and for

others. This has been a field of study for psychotherapy and treatment goals (Singer in (Beike et al. 2004)) and for describing disturbances in schizophrenia (P. H. Lysaker et al. 2005). Disturbances at this level entail the (a) incongruence between one's autobiographical narrative and one's experience (experiencing an existential orientation to an extent that it no longer adapts to previous narrative) and (b) periods of life to which one has experienced but cannot find a narrative for and (c) the occurrence of incidents that don't fit in one's standard narrative. Dissociative identity disorder and borderline personality disorder are said to be examples of pathology of the narrative level of self-experience (S. Gallagher 2011) but also, and here speculative, allowing the person to narrate subjective experiences (by adding them to the psychopathological examination) might increase the congruence between the basic-narrative self and have a therapeutic value.

The second idea, and most important to what is here discussed, is that narratives comprise the accessibility of patients meaning as contingent on (i) his capacity to find words for his experiences (ii) his ability to structure a narrative and (iii) the psychiatrist's aptitude to access the meaning he is portraying. The process of attributing meaning to one's experience is private and persons have both (1) partial arrays of symbols so both the description of being "anxious" might correspond to two different experiences and the description of "nervousness" and "anxiety" can correspond to the same experiential features (2) symbols which are not universally recognized as they are depend on cultural and diachronic changes – e.g. identical experiences might be designated differently, as in *melancholia* of the 19th century Psychiatry, the *sadness* experienced in a farmer, or *depressed mood* said by a psychologist (see more in (Figueira 2015)). Indeed there have been discussions of the idea of "*meaning-complexes*" which are dependent on patients' cultural and social ground (Geertz 1973) (Monti & Stanghellini 1996).

An analysis on patients' *pathological narratives* show their contingency to content and structure of what is narrated. Those can be (1) narratives of psychopathological experiences, (2) situational artifacts (e.g. being shut because of anxiety or shyness) which can also have psychopathological significance and (3) in themselves standing for structural disturbances. The first part is dependent on the problems mentioned in the previous subsection. The second claim regards changes related to setting and situations which entail the problem of *external coherence* that is dependent (1) on the quality of intersubjective setting, (2) shared cultural ground and (3) the landscape of psychiatric assessment (see next section).

The complexity of the last prospect can be presented in the particular case of disordered narratives in SSD where there are at least three prototypes: a disturbance of agency lead to the inability to of building self-referential narratives (Gallagher in (Kircher & David 2003; Graham 2014) fragmented narratives in schizophrenia arise due to a change in temporality and ipseity (Sass & Parnas 2003) and narratives in SSD are the loss of an internal self dialogue which becomes monological (P. H. Lysaker & J. T. Lysaker 2008). Also there seems to exist specificities within each narrative that show deceptive narratives have different structure from true ones (ELISA KRACKOW 2010).

The idea of self-narrative as being important to the understanding of dissociative experiences has also been acclaimed (S. Gallagher & Cole 2011). There are phenomenological specificities to the narratives of dissociative experiences: they are narratives of events that are (1) not experienced but been externally portrayed; (2) experienced as belonging to one's life though the person cannot recall them through a narrative (3) self-consciously detached from usual way of experiencing (4) they are sometimes salient and have a pitch of strangeness while other times show an intrinsic distance between the narrator and the narrated event. The first and second subtypes include episodes of dissociative fugue and amnesia while the third and forth relate to depersonalization and derealization phenomena.

Chapter 2: Prevalence and implications of Truman symptoms in subjects at Ultra High Risk for psychosis

1. Summary

Preliminary qualitative research has suggested that patients in early stages of psychosis and those at Ultra High Risk (UHR) may experience “Truman symptoms” (TS). This arm of the thesis investigated TS in a sample of 26 UHR subjects and 14 matched controls (HC) recruited from three prodromal and early intervention clinics and its relation with clinical features, depersonalization and basic self-disturbances. The UHR were assessed with the Comprehensive Assessment of At-Risk Mental States (CAARMS), Social and Occupational Functioning Assessment Scale (SOFAS), the Positive and Negative Syndrome Scale (PANSS), the Cambridge Depersonalization Scale (CDS) and the Examination of Anomalous Self Experiences (EASE) checklist. In this sample, TS were specific (TS absent in HC) and highly prevalent (50%) in UHR subjects. EASE total scores differed across HC, UHR with TS and without TS (EASE, $H(2)=31.128$, $p<0.001$) but post-hoc analyses showed similar scores in the two latter groups (adjusted $p>0.05$). Despite the sample scores suggesting that HR with and without TS might share the same Anomalous Subjective Self-Experiences other interpretations are discussed. The presence of TS in this UHR sample was associated with higher PANSS general psychopathology score ($t(24)= -2.260$, $p=0.033$) but with no significant difference in the CAARMS, CDS and SOFAS scores. This arm suggested TS that they might be prevalent and specific of UHR subjects.

2. Introduction

Early psychiatric literature portrays the features of impending psychosis as arrangements of depersonalization and derealization (Binswanger 1957; Conrad 1958; Matussek 1952) and operationalized both early by Kurt Schneider in 1st rank symptoms (Schneider 1959) and later by Frank James Fish (Fish, Casey and Kelly 2006). These have been described as changes in the perception of reality, in the understanding of subject's own experiences and in detachment from experience (see a detailed account in (Mishara 2010)) and can be measured on specific psychometric scales such as the Cambridge Depersonalization Scale (CDS) (Sierra & Berrios 2000). These phenomena have been recently symbolized into a new clinical construct denominated "Truman symptoms" (TS) (Fusar-Poli, Howes, et al. 2008) stressing the sense that the ordinary is changed or different and leading towards a "Truman explanation". It refers to the famous 1998 Peter Weir's movie, in which Truman, the protagonist, has lived his life unaware of being in a constructed reality television show and gradually starts to become suspicious of his world (Fusar-Poli, Howes, et al. 2008). TS might be particularly relevant to the psychopathology of UHR group as they: a) are in tune with the dimensional model of psychosis and the possibility of attenuated psychotic symptoms (Fusar-Poli, Howes, et al. 2008) and b) they might apprise the cultural expression of a psychopathological phenomena in this group at young age (familiar with the internet and the virtual reality).

On a psychopathological level, TS are characterized by a profound change of the subjective experience and of self-awareness, resulting in an unstable first-person perspective with varieties of derealization, disturbed sense of ownership, fluidity of the basic sense of identity, distortions of the stream of consciousness and experiences of disembodiment (Fusar-Poli, Howes, et al. 2008). A subject with TS focuses on his sense of self as if ruminating on altered subjective phenomena to which he was previously oblivious. By increasing his self-awareness he focuses and constantly monitors the what, how and why he experiences subjective phenomena. Then, keeping the "as if" component (not a delusion), he might reach a "Truman explanation". Examples of patient quotes can be found in Box 1. TS are conceptually close to the alterations of "basic sense of self" which also include, along others, distortion of first-person perspective, changes in process of thought, the loss of "natural evidence", increased reflexivity and derealization and depersonalization experiences. All the latter have been comprehensively addressed in recent years with detailed descriptions of

each of phenomena (Sass & Parnas 2003; Parnas, Møller, et al. 2005; Zahavi 2000). The disturbances of basic-self also seem to support modern accounts of delusion formation in prodromal and early phases of psychosis that point to a neurobiological underlying alteration in salience processing of stimulus

(Mishara & Fusar-Poli 2013; Roiser et al. 2013; Winton-Brown et al. 2014).

Table 1: Patient Quotes on Truman symptoms

"I'm constantly worrying about me. I wouldn't say I'm persecuted but everything feels oppressive. Take this table or these walls – they're strange. I guess everything looks phony! But its not only here, the walls in my living room also feel paper-like as if I was in a set."
"This started with me thinking rather than feeling. Thinking go the best of me and I started to find it hard to sleep. You can't imagine what is like to know everything is simulated. Having dinner – even at my grandma house! – seems faked!"
"my life feels like a computer game, I know the variables within but I can't set them, surely someone is setting them."
"like The Matrix. Oh… so many times I felt that someone was controlling my world and it was definitely not god. The feeling that things in my world were strangely man-made."
"for the last two years I started this feeling of constant preoccupation. This worrying… is like a permanent dull pain and when I look to others I feel that they know what is happening to me. So many eyes looking at me, you know – like a Big Brother!"

Despite the above observations, that suggest a potential key role of TS in subjects at Ultra High clinical risk for psychosis (HR), particularly the attenuated psychosis symptoms group, their validity as a clinical construct is unknown. First, their occurrence with respect to the UHR state as compared to HC has never been investigated. Second, their impact on presenting UHR symptoms is undetermined. Here are addressed these issues in UHR subjects. The first aim was to measure the prevalence of TS in UHR subjects and matched HC. The second aim was to investigate if TS status affected clinical characteristic of HR, including (i) disturbance of basic self-experiences (EASE), (ii) derealisation and depersonalization phenomena (CDS), (iii) functional status (SOFAS), (iv) UHR symptoms (CAARMS, PANSS). The final aim was to test correlation between these latter items

following a recent research track (Sass, Pienkos, Nelson, et al. 2013) suggesting that the constructs of derealisation and depersonalization and basic self-disturbances could overlap.

3. Material and methods

3.1 Setting and Sample

Participants with Ultra High Clinical Risk for psychosis were enrolled from OASIS (prodromal clinic, SLaM NHS Foundation Trust, London (Fusar-Poli et al. 2013)), West London Early Intervention and CAMEO (Cambridge Early Onset", Cambridge University, Cambridge, UK) Teams. These are well-established prodromal and early intervention clinics for young adults with early symptoms of psychosis. Subjects included in the study were between 18 and 35 years of age. Participants undertook a detailed multidisciplinary assessment including combined review of clinical judgment, screening instruments and semi-structured clinical interviews (Fusar-Poli et al. 2013). The UHR group was defined by High-Risk criteria derived from Comprehensive Assessment of At Risk Mental State (CAARMS) (Yung et al. 2005) and the Social and Occupation Functioning Assessment Scale (SOFAS) (Goldman et al. 1992). In respect to the use of drugs, 65% had never used recreational/illicit drugs, 12.5% had experimented while 15% had moderate to severe use. The UHR sample received medication that included antidepressants (22,5%) and antipsychotics (7,5%). Because of the limited sample size it was not possible to compare these groups. The naturalistic impact of medication on the long term outcomes of the patients has been fully addressed in a separate publication by the group (Fusar-Poli et al. 2015). In their follow-up so far, which ranged from 24-32 months, two of the sample subjects transitioned to a psychotic episode. Healthy controls were recruited locally via advertisement and matched for age and gender. They had no present or past personal psychiatric history and negative family history for psychiatric disorders. The study received ethical approval and all the subjects participated after signing a written voluntary informed consent form.

3.2 Procedure

Two psychiatrists (LM and IB) with strong psychopathological training (including expertise in the EASE checklist) performed the interviews with the instruments detailed below. LM was blind to clinical diagnosis – he was unaware if subjects were HR or controls. LM

performed all interviews (20 of which alone). Inter-rater reliability on the EASE measure was ensured through proper training and combined scoring of tape-recorded interviews. If contrasting scores were recorded at the end of the interviews the final results were obtained through consensus discussion.

3.3 Sociodemographics

Information was collected from the subjects' clinical file on age, gender, country of birth, employment (full time students were considered employed), education, history of psychiatric treatment, family history of psychiatric disorder and duration of symptoms prior to clinic entry, in line with previous OASIS studies (Fusar-Poli et al., 2013). Healthy controls were subject to the same clinical enquiring in a research setting. The sample was recruited between August 2013 and November 2013.

3.4 Clinical Measures

Truman symptoms (TS) (Fusar-Poli, Howes, et al. 2008)

The prevalence of TS in UHR and HC subjects was evaluated clinically as follows. TS were considered present if the following three features were described during the clinical interview i) a sense that the ordinary is changed or different, ii) the subject describes that there is a particular significance leading to 'Truman explanation' all of which is accompanied by one or more of the following iii) a profound alteration of subjective experience and of self-awareness, resulting in an unstable first-person perspective with varieties of derealization, disturbed sense of ownership, fluidity of the basic sense of identity, distortions of the stream of consciousness and experiences of disembodiment. The clinical definition used here is in line with previous account of the TS (Mishara & Fusar-Poli 2013; Fusar-Poli, Howes, et al. 2008). The interviewers solicited patients with open questions on changes on the experience of their world and then directly inquired on all the three criteria above whilst administering the EASE or CAARMS assessment. The third criterion is further detailed in the EASE in the self-awareness and presence domain and the reader can refer to the seminal paper to find a detailed explanation and patient examples of each of the items (see reference below).

Comprehensive Assessment of At-Risk Mental State (CAARMS) (Yung et al. 2005)

This is a semi-structured clinical interview designed to assess attenuated psychotic symptoms (including perceptual and thought disturbances) and represents the core part of the initial assessment of OASIS and CAMEO teams. It consists of 28 items divided through 7 subscales: 4 Positive Symptom items, 2 Cognitive and 3 Emotional Disturbances items, 3 Negative Symptoms items, 4 Behavioral Change items, 4 Motor/Physical Changes items, and 8 General Psychopathology items. The scores were used as a measure of the UHR presenting symptoms. The scores include rating of the severity and frequency of the symptom in a 6-point assessment (from 0 absent/never to 6 psychotic and severe/continuous).

Social and Occupation Functioning Assessment Scale (Goldman et al. 1992)

This scale is a modified version of the Global Assessment of Functioning (GAF) scale separating the measures of social and occupational functioning from the measures of symptoms and psychological functioning. Its scores range from 0 to 100. Scoring is according to information obtained in the psychiatric interview.

Positive and Negative Syndrome Scale (PANSS) (Kay et al. 1987)

This is a seven-point assessment (from absent to extreme) of 30 items across three domains: 7 positive, 7 negative and 16 general psychopathology items. It was used in the study to assess general psychopathology and positive and negative symptoms. It was part of the assessment at admission in the OASIS and CAMEO teams.

Examination of Anomalous Self Experiences checklist (EASE) (Parnas et al., 2005b)

This is a checklist for a semi-structured interview of anomalous subjective experience with 57 items (88 if sub-items are included) and a Cronbach α of 0,87 (Moller et al., 2011). It is divided into 5 domains: a) 28 sub-items on cognition and stream of consciousness; b) 36 sub-items on self-awareness and presence; c) 16 sub-items on bodily experiences; d) 6 sub-items on demarcation/transitivism; e) 8 sub-items on existential reorientation. The overall score was rated dichotomously in accordance with presence (1) or absence (0) of items. It has been shown to be a reliable instrument (Moller et al., 2011) measuring anomalous

experiences of the "pre-reflective" sense of first-person perspective or basic self. These abnormalities of self-awareness have then been shown as promising in the conceptualization of those at risk of psychosis (Nelson et al., 2008) and in schizophrenia-prone individuals (Nelson et al., 2013; Parnas, 2005). Also, they have been empirically substantiated in a) early psychosis (Parnas et al., 2005a), b) prodromal phases of psychosis (Nelson et al., 2012; Parnas et al., 1998; Zahavi, 2000) and c) in the silent side of spectrum of schizophrenia (Raballo and Parnas, 2011).

Cambridge Depersonalization Scale, (CDS) (Sierra & Berrios 2000)

This is a 29 item self-report scale to be used in assessing depersonalization and derealisation experiences including frequency and duration (α 0,89). Frequency of phenomena is rated from 0 (never) to 4 (all the time), while duration is rated from 1 (few seconds) to 6 (more than a week). It was used as an indirect measure and proof of external validity for the "Truman symptoms". The TS was correlated with the overlapping constructs of CDS and EASE (as shown below).

3.5 Statistical Analysis

Descriptive analysis included t-tests for continuous variables and Fisher exact test for categorical variables. Inter-rater reliability was tested by independent reevaluation of the tape recording of the first 6 interviews (three interviews performed by IB and three by LM which were subsequently evaluated by the other interviewer).

The first aim was to measure the prevalence of TS in UHR subjects and matched HC. So in the first analysis was a comparison of the prevalence of TS in UHR subjects and HC. The second aim was to investigate if TS status affected clinical characteristic of HR, including: a) disturbance of basic self-experiences (EASE); b) derealisation and depersonalization phenomena (CDS); c) functional status (SOFAS); d) UHR symptoms (CAARMS, PANSS). Regarding the first three measures, since the assumption of normality and homogeneity of variance were violated (Shapiro-Wilk test significant in at least one group for each variable, $p<0.05$; Levene test significant in every variable but EASE Existential Reorientation subscale, $p<0.05$), here was decided to perform Kruskal-Wallis non-parametric test. It was performed post-hoc pairwise analysis accounting for multiple comparisons. CAARMS and

PANSS scores were compared using t-tests as normality assumption was retained. When not otherwise specified, two-side $p<0.05$ was considered significant and Bonferroni's correction for multiple comparisons was applied. The last aim was to test correlation between CDS and EASE total score in the UHR group. Again, since the normality assumption was not retained, bootstrap (10000 iterations) was performed to compute 95% CI, after visual inspection of scatter plots to exclude potential outliers. All the analyses were performed under SPSS IBM 22.

4. Results

4.1 Sociodemographic characteristics

The interviews in HC took on average 58 (SD 10) and 134 min (SD 40) in UHR subjects. The overall inter-rater correlation of EASE total score was 0.90 ($p<0.001$). The sample consisted of 26 UHR subjects with mean age of 23.73 (SD 4.35) years and of which 57% males. The matching sample of HC participants did not differ in baseline demographics, accounted in **Table 1**, but healthy controls had a higher employment rate than UHR ($p=0.037$).

Table 2: Sociodemographic and Clinical characterization of sample

	Total sample (N=40) mean±SD or n (%)		UHR (n = 26)			
		HC (N=14) mean±SD or n (%)	TS- (N=13) mean±SD or n (%)	TS+ (N=13) mean±SD or n (%)	F or Fisher's	p*
Age at inclusion	23.9±3.9	24.21±3.22	24.46±4.61	23.00±4.02	0.508	p=0.606
Country of Birth						p=0.648
United Kingdom	38 (95)	13 (92.9)	12 (92.3)	13 (100)		
Other	2 (5)	1 (7.1)	1 (7.7)	-		
Gender					3.190	p=0.217
Male	19 (47.5)	4 (28.6)	7 (53.8)	8 (61.5)		
Female	21 (52.5)	10 (71.4)	6 (46.2)	5 (38.5)		
Ethnicity					1.954	p=0.421
White British	24 (60)	10 (71.4)	6 (46.2)	8 (61.5)		
Other	15 (37.5)	4 (28.6)	7 (53.8)	4 (30.8)		
Missing	1 (2.5)	-	-	1 (7.7)		
Employed/ Studying					6.310	p=0.037
Yes	27 (67.5)	13 (92.9)	8 (61.5)	6 (46.2)		
No	12 (30)	1 (7.1)	5 (38.5)	6 (46.2)		
Missing	1 (2.5)	-	-	1 (7.6)		
Mean nº years of Education (years)	14.79±2.90	16.14±3.44	14.38±2.18	13.67±2.46	2.783	p=0.075

number of subjects or Mean ± SD. Percentages under parenthesis.
* p-values refer to ANOVA and Fisher's Exact Test between HC, UHR-TS- and UHR-TS+ group for continuous and categorical values respectively

4.2 Prevalence of TS in HR

TS were absent from all subjects in HC group and present in 50% of the subjects in UHR group. Hereinafter, the acronym UHR-TS+ represents subjects that referred TS, while UHR-TS- represents those that did not.

4.3 CDS, EASE, SOFAS, CAARMS and PANSS scores across groups

There were statistically significant differences in EASE and CDS scores (H(2)=31.1, p<0.001 and H(2)=20.4, p<0.001 respectively) across the three groups of HC, UHR-TS+ and UHR-TS-. According with post-hoc tests (adjusted for multiple comparisons), HC scored lower than UHR-TS- and UHR-TS+ in CDS and EASE, including subscales, with the exception of Existential Reorientation (H(1)=-5.6, p=0.591) and Demarcation/transitivism subscale (H(1)=-5.7, p=0.396) in which there were no significant difference between HC and UHR-TS-. There was no significant difference between UHR-TS- and UHR-TS+ in EASE (H(1)=-10.3, p=0.074), CDS (H(1)=-5.7, p=0.453) and EASE subscales with two exceptions: UHR-TS- showed lower scores than UHR-TS+ on Existential Reorientation (H(1)=-12.5, p=0.014) and Demarcation/transitivism subscales (H(1)=-10.2, p=0.025). The three groups also differed for SOFAS scores on functioning with overall impairment in the two UHR groups as compared with HC (*H*(2) 22.875, p<0.001) but no difference emerged between UHR-TS- and UHR-TS+ (H(1)=-3.5, p=1.000, adjusted for multiple comparisons). Regarding psychotic and general psychopathology, UHR subjects with and without TS were compared using t-test since the sample distribution approximate normality for the scales adopted. No significant difference emerged in the CAARMS (UHR-TS-=33.85±16.42, UHR-TS+=43.54±21.64, t=-1.286 (24), p=0.211) and PANSS total scores (UHR-TS-=48.31±11.72, UHR-TS+=57.31±16.90, t=-1.578 (24), p=0.128). However the UHR-TS- group scored lower on PANSS general psychopathology subscale when compared with UHR-TS+ group (t(24)= -2.260, p=0.033, Hedges'g= 1.39 indicating large effect size). **Table 3** portrays CDS, EASE and SOFAS scores across the three groups while **Table 4** details the differences in the CAARMS and PANSS subscales between UHR-TS- and UHR-TS+. The sample distribution of EASE and CDS total scores in three groups is additionally illustrated in **figure 1 and 2**.

Table 3: Between groups differences in CDS, EASE and SOFAS scores

	HC (N=14) median (range) mean rank		UHR-TS- (N=13) median (range) mean rank		UHR-TS+ (N=13) median (range) mean rank		H(2)	p
CDS score	0.00	(0-10)	33.00	(3-84)	82.00	(35-160)	20.359	<0.001
	6.41		17.39		23.11			
EASE score	0.50	(0-9)	19.00	(6-32)	36.00	(18-83)	31.128	<0.001
	7.68		22.27		32.54			
EASE Cognition and Consciousness	0.00	(0-5)	7.00	(2-15)	14.00	(5-23)	28.604	<0.001
	7.75		23.81		30.92			
EASE Self-awareness and Presence	0.00	(0-4)	12.00	(3-19)	15.00	(7-31)	29.559	<0.001
	7.68		23.58		31.23			
EASE Bodily experiences	0.00	(0-1)	2.00	(0-4)	3.00	(1-15)	23.588	<0.001
	9.82		21.88		30.62			
EASE Demarcation/transitivism	0.00	(0-0)	0.00	(0-1)	1.00	(0-6)	17.910	<0.001
	13.50		19.19		29.35			
EASE Existential Reorientation	0.00	(0-5)	1.00	(0-7)	4.00	(2-8)	18.144	<0.001
	12.79		18.38		30.92			
SOFAS score	91.00	(90-100)	60.00	(51-69)	52.00	(40-70)	22.875	<0.001
	30.00		14.41		10.88			

Median (with range) and mean rank for each group are reported. Three groups were compared and considering the non-normal distribution of data and heterogeneity of variance – the Kruskal–Wallis non-parametric test was adopted.

Table 4: Impact of Truman symptoms on the PANSS, CAARMS scores

	UHR-TS- (N=13) mean±SD	UHR-TS+ (N=13) mean±SD	t (24)	p value
PANSS Positive symptoms	11.31±3.09	14.23±4.36	-1.971	p=0.060
PANSS Negative symptoms	12.62±4.71	11.69±5.04	0.482	p=0.634
PANSS General Psychopathology	24.31±6.40	31.38±9.31	-2.260	p=0.033 *
CAARMS Positive symptoms	7.15±4.24	9.00±3.42	-1.223	p=0.233
CAARMS Cognitive Disturbances	3.0±2.31	2.31±1.70	0.870	p=0.393
CAARMS Emotional Disturbances	3.00±3.06	3.00±3.06	0.000	p=1.000
CAARMS Negative symptoms	4.85±3.05	5.38±3.93	-0.390	p=0.700
CAARMS Behavioral Changes	4.69±4.05	6.85±4.51	-1.282	p=0.212
CAARMS Motor/Physical Changes	1.23±2.20	2.31±4.15	-0.826	p=0.417
CAARMS General Psychopathology	10.00±6.31	14.62±7.05	-1.758	p=0.091

We present the comparison between UHR-TS- with UHR-TS+. * Significant difference (2-sided p<0.05)

Figure 1: Examination of Anomalous Self Experiences Scores HC, UHR-TS- and UHR-TS+ groups.

The three groups differed for total EASE score (N=40, *H(2)=31.128,* p<0.001)

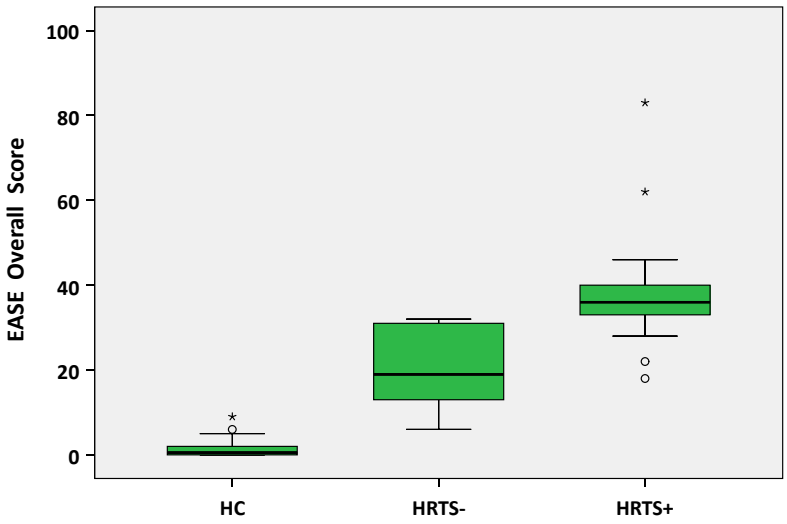


Figure 2: Cambridge Depersonalization Scale scores across HC, UHR-TS- and UHR-TS+ groups

The three groups differed for total EASE score (N=29, *H(2)=31.128,* p<0.001)

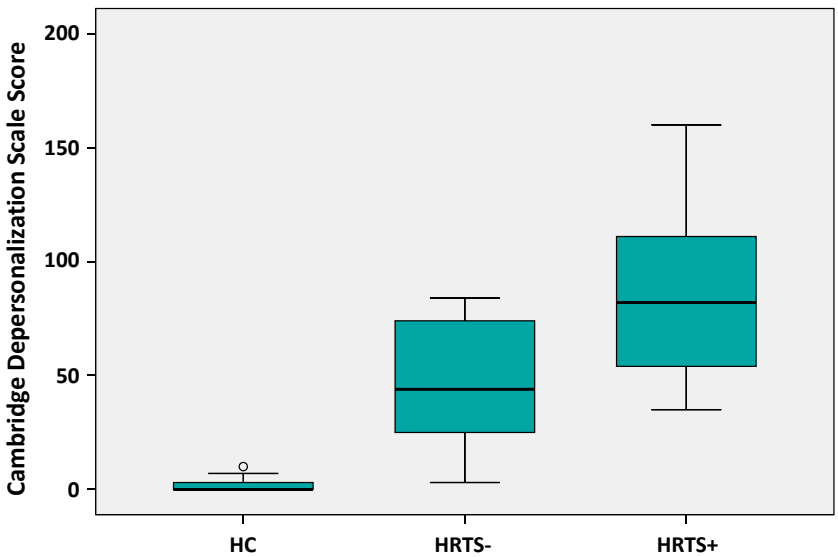
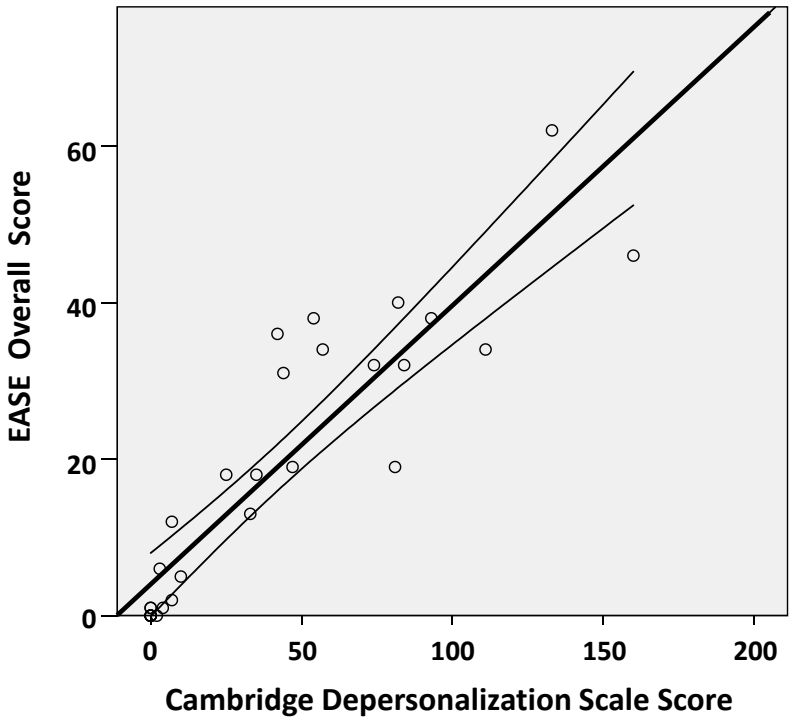


Figure 3: Correlation between EASE and CDS score in the HC and UHR sample

(r=0.902, 95% CI 0.834-0.960, p<0.001 bootstrap method applied)



4.4. Correlation between CDS and EASE in HC and HR

We further tested the relationship between EASE and CDS scores within the sample and found a significant correlation between scores (r=0.902, 95% CI 0.834 - 0.960, p<0.001 bootstrap method applied). Figure 3 represents the correlation between CDS and EASE total scores.

5. Discussion

To my best knowledge this was the first time the prevalence of TS in UHR subjects was investigated. In this seminal exploration, TS appear to be specific and highly prevalent in the UHR sample, as 50% of the UHR subjects experienced TS. Furthermore, in the sample, TS were exclusive to the UHR group empirically suggesting that they might be a phenotypic marker of this state. If the relatively high prevalence of TS found in the UHR subjects was replicated in other UHR samples, the idea that TS might be related to vulnerability to psychosis could be supported. However, as half of the UHR subjects did not present TS they might characterize experiences of a specific subgroup. This would go along with the fact that the UHR group is heterogeneous (Nelson, A. Thompson, Chanen, et al. 2013), with high degree of comorbidity (Fusar-Poli, Nelson, et al. 2014) and pluripotent (Schultze-Lutter et al. 2013) and diverse diagnostic and functional outcomes (Carrión et al. 2013; Fusar-Poli, Nelson, et al. 2014). Prospective studies with larger samples are fundamental to endorse these considerations and to test if TS predicts clinical outcomes in UHR subjects.

The presence of TS in the UHR sample was associated with higher PANSS general psychopathology scores. As with the previous heterogeneity claim, if replicated in larger and longitudinal studies, this result would add clinical value to this cluster suggesting that it might be a "symptom". That is, to hypothesize that TS could be not only a phenomenon occurring in the UHR subjects but also a protagonist in identifying a subgroup of UHR subjects that have higher psychopathology. Contrary to the expectations none of the other clinical measures were impacted by the presence of TS. Indeed, there was no statistical difference in SOFAS, PANNS positive symptoms and CAARMS scores in the sample UHR subjects with or without TS. These results diverge from the clinical consideration that TS matures with a severe disruption of engagement (connection) and enactment (understanding) of reality and is associated with diminished functioning and a change in overall contact with reality (engagement and meaning). Most of these changes would be contained in the PANSS positive symptoms domain which include questions on perception of reality, derealization and perplexity (see relevant conceptualization of delusional mood and perceptual anomalies in (Fuchs 2005a)). The first possible speculation is that all of these negative findings are due to a type II error. An alternative hypothesis, stands upon the possible lack of sensitivity of the PANSS to measure attenuated and moderate psychotic symptoms sufficiently which distress the UHR subjects (Fusar-Poli, Yung, et al. 2014). However the latter explanation is

weakened as the CAARMS and the SOFAS are specific instruments for the UHR psychopathology and the TS status did not differentiate the UHR group in any of the CAARMS specific domain scores neither in their SOFAS scores. However, it is possible to argue that the CAARMS is focused on positive symptoms and does not investigate abnormalities of self-awareness; therefore such non-psychotic alterations may not be reflected in the instrument's scores.

We also investigated basic self-disturbances, as assessed by the EASE total score that had been shown to be relevant for the overall risk of psychosis in the UHR group (Nelson et al. 2009; Nelson, A. Thompson, Chanen, et al. 2013; Nelson et al. 2012). In this UHR sample similar scores of basic self-disturbances were found in subjects with or without TS. These results might represent a false negative due to the small sample size as it was expected higher overall scores in subjects with TS or they can result from the lack of clear message or grasp of this heterogeneous and complex variable (TS). Here was envisioned that the group with TS would have more severe self-awareness impairment and thus more prone to a disruption of engagement and understanding of reality. Yet these findings also allow the understanding in which TS and basic self-disturbances constructs occur in specific and not overlapping cohorts of UHR subjects. This assessment showed that scores of the demarcation/transitivism and existential reorientation EASE subscales were higher in subjects with TS. Only longitudinal studies could sustain this relation and if a specific combination of basic self-disturbances occur in subjects with TS. However, even if it was possible, eventually, to ascertain this extra care must be taken as the existential reorientation domain of the EASE scale includes items that are similar to the TS construct.

Another unexpected result was the average CDS score in the UHR risk group across their TS status. I expected higher scores in the subjects with TS due to the overlap of many of CDS items with the TS construct – e.g. "what I see looks 'flat' or 'lifeless', as if I were looking at a picture" or "my surroundings feel detached or unreal, as if there was a veil between me and the outside world" (Sierra & Berrios 2000). Again if I do not interpret these results as a false negative (either for sample size or the complexity of this variable), I can hypothesize that derealization and depersonalization experiences could lead to other subjective interpretations than the TS cluster. Indeed this would support the idea that TS are singular (and therefore clinically relevant) and that they are not just non-specific depersonalization

and derealization experiences found in anxiety (Sierra et al. 2012), depression (Mula et al. 2007) or even trauma in general (Ludwig 1983).

The third aim was to examine the correlation between the CDS and EASE scores to better understand the relation between derealization and depersonalization experiences and basic self-disturbances in the UHR population. Whilst derealization and depersonalization are taken to be non-specific, basic self-disturbances have been conceptualized as the core feature of the schizophrenic spectrum, and are therefore useful in distinguishing diagnostic outcomes (Nelson, A. Thompson, Chanen, et al. 2013; Parnas et al. 2011). In the whole UHR sample these two domains were closely related. This finding adds up to the idea that there could be an overlap in the portrayal of these phenomena. Indeed the results emphasize the word of caution which was recently put forward regarding the lack of phenomenological detail to separate "true basic self disturbances" from otherwise unspecified depersonalization and derealization experiences (Sass, Pienkos, Nelson, et al. 2013). At a phenomenological level, a full overlap would render narratives of general derealization and depersonalization experiences an important confounding factor to narratives suggesting disturbances of "basic-self" (and schizophrenia proneness). A partial overlap, where a specific domain of CDS experiences is more prevalent in those describing high levels of "basic-self" disturbances, would maintain the idea that there is something particular to the derealization and depersonalization occurring in schizophrenia. Further studies might help clarify this question including those investigating the occurrence "basic-self" disturbances in other clinical populations (e.g. anxiety disorders) and their overlap with general derealization and depersonalization experiences.

6. Limitations

This study is limited by the small sample size and it should be considered exploratory. Here are listed several major limitations: (1) it cannot be dismissed that these results are false negatives or false positives due to the sample size; (2) that there is a conceptual and empirical heterogeneity of the UHR construct (Fusar-Poli, Yung, et al. 2014) that can further impair the use of these results for other UHR populations (3) that the assessment of TS needs to be replicated in other UHR findings to allow generalizability of results; (4) that the differences in employment rates are a possible confounding factor to the results, yet they seemed to us represent an artefact of the process of selection of the UHR group (the use of SOFAS for

functioning); (5) that there are no follow up results, which would help to better define the clinical relevance of TS - they could clarify if TS are general experiences (accounting for anxious and depressive symptoms) or indeed associated with specific experiences at the core of psychosis proneness, (6) that the lack of a clinical control group (e.g. affective, anxious or personality disorders); (7) that although the use of prescribed drugs and of illicit substances was systematically appraised, their effect on the results could not be determined due to small numbers (we have fully investigated these issues in a separate publication (Fusar-Poli et al. 2015); (8) that here TS were not analysed in light of cultural influences. For example the Truman explanation could be a modern way to conceptualize the experience influenced by social media or TV - an analysis of these factors could perhaps allow us to understand if TS are specific to a subset of UHR subject intensely using social media and watching TV shows; (9) that only two UHR clinics were used and the prevalence of UHR in the population might be limited by the specifics of the population. On a personal note, the author takes that TS is a complex and heterogenous variable which, for times, needed comprehensive discussion of all its details in order to obtain true joint understanding – limiting the unrestricted use of the variable in clinical practice as well as might restraining the results of this arm of the study.

7. Partial Synthesis

This is the first study to explore the prevalence and implications of Truman symptoms in a UHR population. TS were prevalent in in this UHR sample and were absent in matched HC's. The UHR subjects with TS had similar scores to the UHR without TS in the EASE, SOFAS, CDS, CAARMS, PANSS, with the exception of higher score on Existential Reorientation and Demarcation/transitivism EASE subscales and General Psychopathology PANSS subscale in the UHR-TS+ group. Within the whole UHR sample, EASE and CDS scores were correlated. Future studies, both prospective and with larger samples, are fundamental to endorse these considerations and to test if TS predicts clinical outcomes or treatment response in UHR subjects.

Chapter 3: Abnormal Bodily Phenomena in subjects at High Clinical Risk for Psychosis

1. Summary

Contemporary phenomenological research has considered abnormal bodily phenomena (ABP) to be a phenotypic trait of subjects with schizophrenia in their first psychotic episode. Yet the prevalence of ABP and their clinical significance in subjects at High-Risk (HR) of psychosis remains unidentified. This study is an exploratory investigation of ABP in HR subjects and matched healthy controls (HC) examining their relation to clinical features and basic self-disturbances. Here is tested a sample of 26 HR and 14 HC subjects from three prodromal and early intervention clinics in South London, West London and Cambridge was assessed with the Abnormal Bodily Phenomena questionnaire (ABPq), Comprehensive Assessment of At-Risk Mental States (CAARMS), the Positive and Negative Syndrome Scale (PANSS), the Social and Occupational Functioning Assessment Scale (SOFAS) and the Examination of Anomalous Self Experiences (EASE) checklist.

In this sample, ABP occurred in 73.1% of HR subjects and prominent ABP (proABP) were referred in 53.8% of them. No HC subject reported ABP. The HR group with proABP had lower CAARMS total score (t=-9.265, p=0.006). There were no differences in PANSS total score (t=-1.235, p=0.277), SOFAS score (H(2) 22.27, p=0.666) and EASE total scores (z=8.565, adjusted p=0.185) in the HR subjects with prominent ABP versus those that did not. This initial investigation suggests that ABP could be a prevalent phenotypic feature of HR subjects and the clinical implications of this are discussed.

2. Introduction

Abnormal bodily phenomena (ABP) have been examined in patients with psychosis and particularly schizophrenia even in their seminal representations (Jaspers 1963). ABP are considered to include several different types of symptoms: disturbed *coenesthesia* (an assortment of uncanny bodily feelings with or without delusional interpretation), kinesthetic hallucinations and disruptions of body structure and boundaries. As a group, ABP are subjective phenomena that may be quasi-ineffable in nature and until recently they have been absent from diagnostic textbooks as we lack sensible, specific and reliable tools to assess them.

Following increasing evidence of the limitations of standardized criteria as well as fully structured interviews (Stanghellini 2009a) (Nordgaard et al. 2013), the development of phenomenologically-based, semi-structured interviews has allowed a better insight into subjective phenomena (Parnas et al. 2008). This is the case of the EASE interview (Parnas, Handest, et al. 2005) which focuses on anomalous subjective self experiences (ASE), the use of which has become increasingly relevant in research on psychosis (Møller et al. 2011) and schizophrenia (Sass 2003) (Parnas, Handest, et al. 2005). The concept of "self" has brought about major interdisciplinary interaction aiming to find common conceptual ground for research. One of the present conceptions takes the self as a pyramidal structure with three elements: the pre-reflexive (the "basic" experiences which implicitly compose one's way of being in the world), reflexive (the cognitive appraisal of oneself and the world) and narrative (the autobiography which one narrates when portraying oneself). The three elements are interlinked in such a way that a disturbance in pre-reflexive experience of the self could lead to disturbances of other levels of self-experience. There are major inputs to this conception from various authors including Joseph Parnas, Louis Sass, Dan Zahavi and Shaun Gallagher (Sass 2013; S. Gallagher 2011; Sass 2003; Zahavi 2014; Kircher & David 2003). The "Anomalous self-experiences" selected by the EASE are an heterogeneous group of phenomena which involve symptoms such as: subjectively experiencing a disturbed way of thinking, subjectively experiencing a disturbed way of being in the world, subjectively experiencing disturbances to one's own body, disturbances in interpersonal relations and disturbances in principles and attitudes to the world. The EASE interview has shown a good internal and external validity and its use in subjects at high-risk of psychosis (Nelson et al. 2012; Nelson et al. 2009; Nelson, A. Thompson, Chanen, et al. 2013; Nelson, A. Thompson

& Yung 2013) and in prodromal phases of schizophrenia (Parnas 2005; Nelson et al. 2012) has shown that ASE are present in these populations and suggested they could be used as an early marker.

Table 5 Example of Abnormal Bodily Phenomena (sample)

Experience of violation "when he stretched his hand I felt an energy entering my body. That energy was pounding my right side until it break in"
Experience of externalization "I felt that my body had become as a boiling soup and I was no longer in control of my energy that flows around me. Then my body became an ingredient in the soup parts of me are the vapors and rest of the soup "
Morbid objectivization "I felt my brain freezing. Then thoughts were moving so slowly I could feel them drive from ear to ear"
Devitalization "The loss of the animal part in me, I lost it! I feel that I act as I was programmed, even eating and I feel like a robot, even my arms feel artificially attached to me"
Experience of internal dynamization "I felt my brain starting to rotate, only slightly, but to a point where I was worried it would detach from my neck and it was going to fall to the floor"
Experience of transformation "I felt that my hands were shifting as I moved them towards my face – bigger than smaller. Such a scary sense that I had to look away"
Dysmorphophobia "I always felt my left part of my body was not ok. I even wondered that it might not be mine. There is a sense of evil from the left side. I feel that it's evil"
Disesthesic paroxysm "blurring feeling on my cheek and neck when someone speaks to me. I cannot describe it but its sufficiently awkward for me to be scared of being too close"
Recurrent pain-like experience "the pain just comes and goes… normally when I'm breathing I can end up feeling needles in the lung. I know wrong kind of pain as its so different. it doesn't help taking anything"

A similar research track has now explored the prevalence and relevance of ABP in patients with first psychotic episode and, in particular, in subjects with diagnosis of schizophrenia (Stanghellini et al. 2012) (Stanghellini, Ballerini, Blasi, et al. 2014). The "Abnormal Bodily Phenomena Questionnaire" (ABPq) (Stanghellini, Ballerini & Cutting 2014; Stanghellini, Ballerini, Blasi, et al. 2014) allows a systematized enquiry in to these experiences. Studies using ABPq have shown an assortment of bodily phenomena occurring in schizophrenia (Stanghellini, Ballerini, Blasi, et al. 2014) and the in the first episode psychosis (Stanghellini et al. 2012). These include uncanny feelings of numbness, loss of body vitality, the sense of disappearance of parts, change in form (shrinking or enlargement), dimension unusual heaviness or lightness) or even "movement of internal parts" of the body

(Ey 1973; Stanghellini et al. 2012; Dupré 1925). Examples of these phenomena are presented in the **Table 4.**

Various studies suggest that ABP occur as trait features before the first psychotic episode in patients with schizophrenia (Hemsley 1998; Klosterkötter et al. 2001; Röhricht & Priebe 2002; Stanghellini 2009b; Schultze-Lutter, Ruhrmann, et al. 2007; Gallese & Ferri 2013). The Comprehensive Assessment of At-Risk Mental State scale [31], one of the instruments relevant to the HR profile, also selects disturbances of bodily phenomena. Yet no study has independently regarded their presence and clinical significance in subjects at high-risk of psychosis. Therefore their occurrence and phenotypic profile is unknown, as is their relation with other presenting symptoms.

This study used the ABPq to appraise ABP in a sample of subjects at High Risk of Psychosis (HR) and assess their occurrence in this population. The first goal was to measure the prevalence of ABP in HR group and matched healthy controls (HC). The second goal was to see how the presence of ABP was related to other clinical features in this population including (i) functional features (SOFAS), (ii) HR symptoms (PANSS and CAARMS) and (iii) disturbance of basic self-experiences (EASE).

3. Methods

3.1 Setting and sample

This sample included subjects at High Clinical Risk for psychosis from OASIS (prodromal clinic, SLaM NHS Foundation Trust, London (Fusar-Poli et al. 2013)), West London Early Intervention and CAMEO ("Cambridge Early Onset", Cambridge University, Cambridge, UK) teams. These clinics are responsible for early intervention in young adults where they undertake a detailed multidisciplinary assessment including combined review of clinical judgment and screening instruments (Fusar-Poli et al. 2013). The ABP and EASE semi-structured clinical interviews were added. Their HR group is defined by High-Risk criteria derived from Comprehensive Assessment of At Risk Mental State (CAARMS) (Yung et al. 2005) and the Social and Occupation Functioning Assessment Scale (SOFAS) (Goldman et al. 1992). Some features of the sample included: subjects were between 18 and 35 years of age, 65% of the subjects had never used drugs while 12.5% had experimented and 15% had

moderate to severe use 22.5% were taking antidepressants while 7.5% were taking antipsychotics. After an average of 28 months of follow-up (November 2015) two of the HR subjects transitioned to a psychotic episode. Enrollment process for controls included advertisement for those matched for age and gender subjects and that had no present or past personal or family psychiatric history. This study had ethical approval and all the subjects participated after signing a written voluntary informed consent form.

3.2 Procedure:

In this study, detailed semi-structured interviews were performed by two psychiatrists (LM and IB) blind to clinical diagnosis. They have strong training in Psychopathology and a cthese in using the EASE (semi-structured interview similar to the Abnormal Bodily Phenomena questionnaire). Joint scoring of audio-recorded interviews ensured inter-raters reliability. The final scores were decided through consensus discussion.

3.3 Sociodemographics

In line with previous OASIS studies, socio-demographic data was collected from the subjects' clinical file. These included age, gender, education, personal or family history of psychiatric disorder and present or past psychiatric treatment, country of birth and employment (full time students were considered employed). (Fusar-Poli et al. 2013). Healthy controls were asked the same questions during the interviews. The sample was recruited between August 2013 and November 2013.

3.4 Clinical Measures

Anomalous Bodily Phenomena Questionnaire (ABPq) (Stanghellini, Ballerini & Cutting 2014)

The prevalence of ABP was assessed with the ABPq, a nine items semi-structured interview split into five sections: Demarcation (experience of violation and externalisation), Vitality (morbid objectivisation and devitalisation), Coherence (experience of internal dynamisation), Identity (experience of transformation and dysmorphophobia) and Activity (disesthesic paroxysm and recurrent pain-like experiences). Each item is scored for its frequency, intensity, impairment and coping in 7 point assessment scale. The developers of

ABPq proposed that we should acknowledge the overall score as the sum of all scores and the presence of "prominent ABP" (proABP) in subjects with scores over 3 in any of the domains. Selected examples of patients' answers are present in the introduction textbox.

Positive and Negative Syndrome Scale (PANSS) (Kay et al. 1987)*:*

A seven-point assessment of 30 items split into three sections: 7 positive, 7 negative and 16 general psychopathology items. It was part of the assessment at admission in the OASIS and CAMEO teams. In this study it allowed the assessment of general psychopathology and positive and negative symptoms and their relation to ABP.

Comprehensive Assessment of At-Risk Mental State (CAARMS) (Yung et al. 2005)

A semi-structured clinical interview for attenuated psychotic symptoms (thought disturbances and perceptual abnormalities), which is part of the assessment of OASIS and CAMEO teams. It has 26 items divided across 7 subscales: 4 Positive Symptom items, 2 Cognitive and 3 Emotional Disturbances items, 3 Negative Symptoms items, 4 Behavioral Change items, 4 Motor/Physical Changes items, and 8 General Psychopathology items. These are rated on severity and frequency of the symptom in a 6-point assessment (from 0 absent/never to 6 psychotic and severe/continuous).

Social and Occupation Functioning Assessment Scale (SOFAS) (Goldman et al. 1992)

This scale is a modified version of the Global Assessment of Functioning (GAF) scale separating the measures of social and occupational functioning from the measures of symptoms and psychological functioning. Its scores range from 0 to 100. Scoring is according to information obtained in the psychiatric interview.

Examination of Anomalous Self Experiences checklist (EASE) (Parnas, Møller, et al. 2005)

It is a semi-structured interview for anomalous subjective experience that includes 57 items (88 if sub-items) and a Cronbach α of 0,87 (Møller et al. 2011). It is divided into five subscales a) 28 sub-items cognition and stream of consciousness; b) 36 sub-items in self-awareness and presence; c) 16 sub-items in bodily experiences; d) 6 sub-items in demarcation/transitivism; e) 8 sub-items in existential reorientation. The score was an

overall dichotomous score in accordance to presence (1) or absence (0) of items. It is a reliable instrument to inquiry anomalous experiences of the "pre-reflexive" sense of first-person perspective or basic self (Møller et al. 2011). They have been empirically substantiated in a) early psychosis (Parnas, Handest, et al. 2005), b) prodromal phases of psychosis (Parnas et al. 1998; Nelson et al. 2012) and c) in the schizotypic and those with schizotaxia (Raballo & Parnas 2011). The abnormalities of self-awareness have been shown as promising in the conceptualization of those at risk of psychosis (Nelson et al. 2008) and in schizophrenia-prone individuals (Parnas 2005; Nelson, A. Thompson & Yung 2013).

3.5 Statistical Analysis

Descriptive statistics including ANOVA and t-tests for continuous variables and Fisher exact test for categorical variables were used to compare between group differences. Non-parametric tests were used as appropriate when the assumptions for parametric null hypothesis tests were violated. Here inter-rater reliability was tested by independent reevaluation of the tape recording of the first 6 interviews (three interviews performed by IB and three by LM which were subsequently evaluated by the other interviewer).

The first aim was to measure the prevalence of ABP and proABP in HR subjects and matched HC. The second aim was to investigate if the presence of proABP affected clinical features of HR including a) HR symptoms (CAARMS and PANSS scores), b) functional status (SOFAS score) and c) disturbance of basic self-experiences (EASE score). For CAARMS and PANSS scores, as normality assumption was maintained, t-tests were used to compare HRproABP- or HRproABP+ groups. For SOFAS and EASE scores, as the assumption of normality and homogeneity of variance were violated (Shapiro-Wilk test significant in at least one group for each variable, $p<0.05$; Levene test significant in every variable but EASE Existential Reorientation subscale, $p<0.05$) so Kruskal-Wallis non-parametric test was chosen to compare HC, HRproABP- and HRproABP+. For post-hoc analysis Dunn-Bonferroni's approach (Dunn 1964) was used for multiple comparisons in non-parametric test. When not otherwise specified, two-side $p<0.05$ was considered significant. Given the exploratory nature of this study and the small sample size, it was decided not to control for familywise error rate. This decision was made to avoid loss of statistical power. However, here was also performed a Bonferroni correction in the post-hoc analysis given the large increase in the number of null hypothesis formulated in this

procedure. The adjusted p-value (p * number of pairwise comparisons) has been reported. All the analyses were performed under SPSS IBM 22.

4. Results

4.1 Sociodemographic characteristics

Interviews took on average 58 min (SD=10) in HC and 134 min (SD=40) in HR subjects. The inter-rater correlation was 0.90 ($p<0.001$) overall. The sample comprised 26 HR subjects with mean age of 23.73 years (SD 4.35) and of which 57% were male. The matching sample of HC participants presented no differences on baseline demographics, accounted in **Table 6**, but the employment rate was higher in HC than HR (Fisher's exact test 6.983, p=0.029).

Table 6: Socio-demographic and clinical characterization of sample

	Total sample (N=40) mean±SD or n (%)	HC (N=14) mean±SD or n (%)	HR (n = 26) HRproABP- (N=13) mean±SD or n (%)	HRproABP+ (N=14) mean±SD or n (%)	F or Fisher's	p
Age at inclusion	23.9±3.9	24.21±3.22	23.25±4.070	24.14±4.605	0.227	p=0.798
Country of Birth					1.107	p=1.000
United Kingdom	38 (95)	13 (92.9)	12 (100)	13 (92.9)		
Other	2 (5)	1 (7.1)	-	1(7.1)		
Gender					3.048	p=0.236
Male	19 (47.5)	4 (28.6)	7 (41.7)	8 (57.1)		
Female	21 (52.5)	10 (71.4)	5 (23.8)	6 (42.9)		
Ethnicity					1.014	p=0.707
White British	24 (60)	10 (71.4)	7 (58.3)	7 (53.8)		
Other	15 (37.5)	4 (28.6)	5 (41.7)	6 (46.2)		
Missing	1 (2.5)	-	-	1 (7.7)		
Employed/ Studying					6.983	p=0.029
Yes	27 (67.5)	13 (92.9)	8 (66.7)	6 (46.2)		
No	12 (30)	1 (7.1)	4 (33.3)	7 (58.3)		
Missing	1 (2.5)	-	-	1 (7.6)		
Mean nº years of Education (years)	14.78±2.91	16.14±3.44	15.08±1.83	13.04±2.33	4.565	p=0.017

number of subjects or Mean ± SD. Percentages under parenthesis. p-values refer to ANOVA and Fisher's Exact Test between HC, HRproABP- and HRproABP+ group for continuous and categorical values respectively

4.2 Prevalence of ABP and proABP and average ABPq score

In this sample, ABP were absent in all subjects in HC group and were found in 19 (73.1%) HR subjects where its overall score (mean, SD) was 35.43±35.80. These represent subjects with several ABP, which they evaluated in their frequency, intensity and impairment and to which they discussed the coping strategies. Regarding the individual domain scores, HR sample subjects reported (mean±SD) a disturbance in ego demarcation score of 4.84±9.76, a disturbance in ego vitality score of 9.0±10.47, a disturbance in ego coherence score of 3.00±6.26, a disturbance in ego Identity score of 8.05±12.86 and a disturbance in ego activity score of 10.53±9.36. The scoring system allowed the identification of 14 subjects (53.8%) with prominent ABP and hereinafter the acronym HRproABP+ represents these subjects while HRproABP- represents those that had no ABP or that considered them mild.

4.3 EASE, SOFAS, CAARMS and PANSS scores across HC, HRproABP+ and HRproABP- groups

There were statistically significant differences in EASE total and specific scores across the three groups of HC, HRproABP- and HRproABP+. **Table 7** portrays EASE and SOFAS scores across HC, HRproABP- and HRproABP+ groups. The post-hoc analysis between HRproABP- and HRproABP+ groups showed no differences between their SOFAS score (z=-1.371, p=1.00) and their EASE total score (z=8.565, adjusted p=0.185). **Figure 4** displays sample distribution of EASE scores across HC, HRproABP- and HRproABP+ groups.

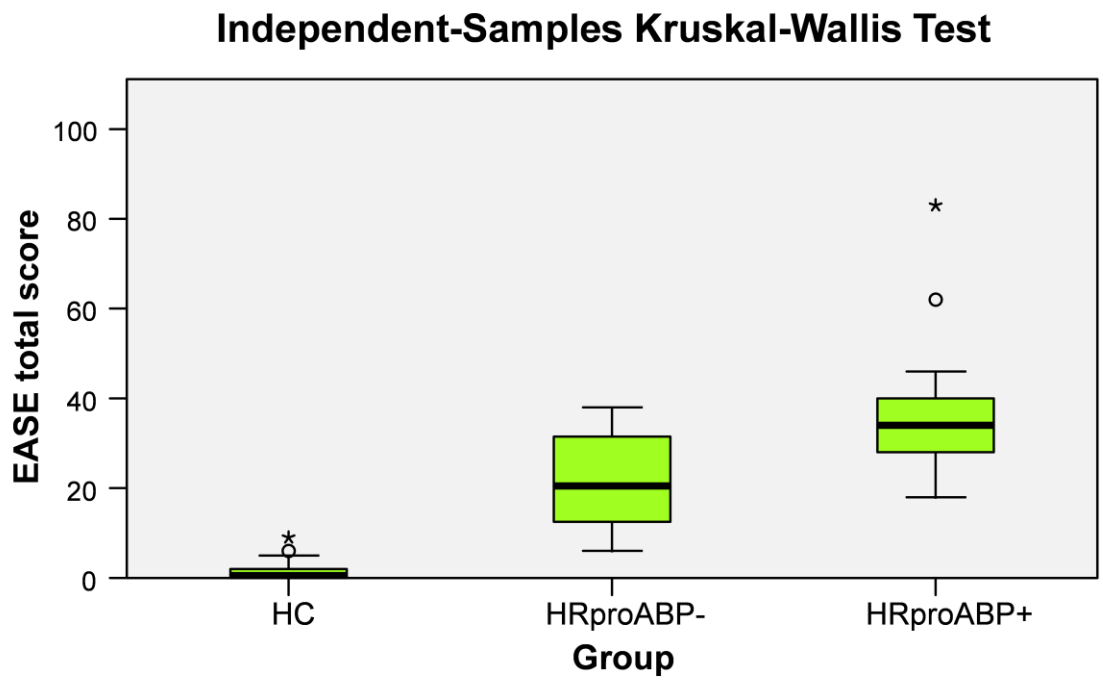
Table 7: Between groups differences in EASE and SOFAS scores

	HC (N=14) median (range) Mean rank	HRproABP- (N=12) median (range) Mean rank	HRproABP+ (N=14) median (range) Mean rank	H(2)	p
EASE score	0.50 (0-9) 7.68	20.50 (6-38) 22.79	34.00 (18-83) 31.36	29.570	p<0.001
EASE Cognition and Consciousness score	(0-5) 7.75	7.00 (2-15) 23.50	13.00 (5-23) 30.68	28.634	p<0.001
EASE Self-awareness and Presence score	0.00 (0-4) 7.68	11.00 (3-19) 24.50	13.50 (6-31) 29.89	28.105	p<0.001
EASE Bodily experiences score	0.00 (0-1) 9.82	1.50 (0-4) 20.83	3.50 (1-15) 30.89	24.854	p<0.001
EASE Demarcation/ transitivism score	0.00 (0-0) 13.50	0.00 (0-1) 21.21	1.00 (0-6) 26.89	13.121	p=0.001
EASE Existential Reorientation score	0.00 (0-5) 12.79	0.50 (0-7) 19.33	4.00 (1-8) 29.21	15.065	p=0.001
SOFAS score	91.00 (90-100) 30.00	60.00 (40-75) 11.70	59.00 (43-70) 13.07	22.270	p<0.001

Three groups were compared and considering the non-normal distribution of data and heterogeneity of variance, the Kruskal–Wallis non-parametric test was adopted. Median (with range) and mean rank for each group are reported. P values correspond to differences between the three groups. Abbreviations: HC: Healthy controls; HRproABP+: HR subjects with prominent ABP; HRproABP-: HR subjects with no prominent ABP

Figure 4: Examination of Anomalous Self Experiences Scores in HC, HRproABP- and HRproABP+

The three groups differed for total EASE score (N=40, H(2)=29.570, p<0.001)



In the sample the HRproABP+ vs HRproABP- subjects had on average lower CAARMS total score (HRproABP- 41.42±12.32, HRproABP+ 36.36±24.23, t=-9.265 (24), p=0.006). There were no statistically significant differences in PANSS total score between those groups (HRproABP-=51.33±12.72, HRproABP+=54.07±17.04, t=-1.235 (24), p=0.277). **Table 8** details the differences between PANSS and CAARMS specific domain scores across HRproABP+ and HRproABP- groups.

Table 8: Impact of proABP on the PANSS and CAARMS scores

	HRproABP- (N=12) mean±SD	HRproABP+ (N=14) mean±SD	t (24)	p value
PANSS Positive Symptoms	12.17±3.90	13.29±4.14	-0.705	p=0.487
PANSS Negative Symptoms	12.25±4.84	12.07±4.95	0.093	p=0.927
PANSS General Psychopathology	26.83±7.15	28.81±9.89	-0.547	p=0.589
CAARMS Positive Symptoms	8.83±4.46	7.86±3.48	0.306	p=0.762
CAARMS Cognitive Disturbances	3.50±1.93	1.93±1.82	2.111	p=0.045*
CAARMS Emotional Disturbances	3.08±2.93	2.93±2.98	0.129	p=0.899
CAARMS Negative symptoms	6.25±3.36	4.14±3.35	1.597	p=0.123
CAARMS Behavioral Changes	5.58±3.75	5.93±4.92	-0.198	p=0.844
CAARMS Motor/Physical Changes	1.17±2.29	2.29±3.99	-0.857	p=0.400
CAARMS General Psychopathology	13.50±5.99	11.29±7.80	0.802	p=0.430

* Significant difference (2-sided p<0.05)

5. Discussion

This is a preliminary study exploring the prevalence and the impact of ABP on other clinical features in HR subjects. In the sample, ABP were specific and highly prevalent in HR subjects - more than half of the HR subjects showed prominent ABP. There were significant differences in EASE scores across HC, HRproABP- and HRproABP+. Yet subjects with prominent ABP (versus other HR subjects) only differ in their CAARMS overall score (which was lower) while they did not in their EASE total, PANSS and SOFAs scores. Prospective studies with larger samples are fundamental to endorse these considerations and to test if ABP predicts clinical outcomes in UHR subjects."

The first aim was to determine if ABP were present in the HR subjects. 73% of these sample subjects experienced ABP and ~53% experienced prominent ABP. This feature contrasted with HC group that reported no ABP. This allowed the speculation that ABP might be a phenotypic marker of psychosis vulnerability, which only further studies with larger samples and with clinical control group can show. Still, as much as 30% of the sample had no ABP and 50% had no prominent ABP. This seems attuned to the fact that the HR is heterogeneous, presents various comorbidities and has diverse diagnostic and functional outcomes [13].

The second aim was to determine if ABP impacted on clinical features of the HR population. The presence of proABP status did not differentiate the HR sample across PANSS and SOFAS scores and that proABP subjects had lower CAARMS overall score. Again due to the small sample size in the study, the ABP value as a clinical feature remains unknown. Yet the lower CAARMS scores made us raise the possibility that ABPq might assess phenomena unlike other criteria defining HR for psychosis (including bodily phenomena considered in the CAARMS) as 50% of the HR sample had prominent ABP and lower CAARMS score was found.

The third aim was to test the relation between ABP and anomalous subjective self-experiences. The HR group had higher EASE scores compared to controls. This is in line with previous evidence showing the presence of ASE in the HR group (Nelson et al. 2012; Nelson et al. 2009) and the possibility that they segregate the HR subjects at risk of schizophrenia (Nelson, A. Thompson & Yung 2013). In the sample subjects referring prominent ABP did not have significantly higher EASE scores. This may be due to weak

statistical power due to small group size in each group and further studies with larger samples are need to clarify this issue. It should not be understated that the relation between ABPq and EASE interview also occurs at phenomenological level and it is important to elucidate if they are overlapping constructs or if one is a sub-construct of the other. There are studies suggesting that ASE lead to ABP (Kircher & David 2003) while others advocate that ABP antecede the occurrence of ASE (Scharfetter 1981; Kato & Ishiguro 1997). This "causative relation" is yet to be clarified and needs further investigation. It seems important to stress that the bodily phenomena assessed by the ABPq and the EASE interview are different – for instance "internal dynamism" item only appears in the first and the "mirror-effect" is only materialized in the second – and might carry distinctive implications. An overall better conceptualization of the mutual implications between ABP and ASE is needed.

6. Limitations

First, due to the small sample size, the study should be considered as an exploratory study. It is not possible to exclude that the results could be false negatives or false positives. The generalization of the results might be limited by the specifics of the sample as only two HR clinics were used. Along these limitations, which are specific to the study, it must be considered that the HR construct has shown conceptual and empirical heterogeneity further limiting the relevance of the results to other HR populations (Schultze-Lutter et al. 2013). The difference in employment rates across the sample groups seemed to be an artefact of the process of selection of the HR group (the use of SOFAS for functioning). A clinical control group (e.g. affective, anxious or personality disorders) and follow-up data are necessary to better define the clinical relevance of ABP. Lastly, prescribed drugs and illicit substances were appraised and yet the small sample size did not allow the determination of their effect on the scores.

7. Partial Synthesis

This is the first study to explore the prevalence and implications of Abnormal Bodily Phenomena in subjects considered at high risk of psychosis. In the HR sample ABP were highly prevalent (while absent from matched HC) and in 50% of subjects prominent ABP were found. It raised the possibility that ABP could be a phenotypic component of HR psychopathology and particularly of a subgroup of these subjects. Future prospective and

with larger samples studies are necessary before endorsing these considerations and particularly, to understand if ABP predicts clinical outcomes or treatment response in HR subjects.

Chapter 4: Basic-self disturbances in Panic Disorder

1. General Summary

A key purpose of the present arm of the study — the first to examine anomalous self-experiences (ASEs) in panic disorder — is to begin exploring this self-related dimension of anxiety disorders. Another is to help clarify precisely what might, or might not, be specific to the schizophrenia-spectrum domain (where ASE has previously been identified) — which, in turn, could be useful for developing pathogenetic models for various disorders. Here was recruited a sample of 47 Panic Disorder (PD) patients (with follow-up at a Hospital Outpatient Clinic) and 47 healthy control (HC) subjects from the North Lisbon Central Hospital (C.H.L.N.), which was assessed with the Examination of Anomalous Self Experiences (EASE) checklist and Cambridge Depersonalization Scale (CDS). This arm of the study reports that all patients in the PD sample had ASE and their EASE scores were significantly higher than in the HC (17.94± SD 11.88 vs HC 1.00± SD 1.81). This PD sample also had much higher EASE scores than those found in previous EASE studies of bipolar psychosis or other mental disorders (averages of 6.3 and 8.1, $p<0.005$), though somewhat lower than scores found in previous EASE studies of schizophrenia-spectrum patients (average EASE scores of 25.3, 21.4, 19.6, $p<0.005$). The distribution of EASE items and sub-items in the PD sample was heterogeneous, varying from rare (<10%) or absent (termed "discrepancies" with schizophrenia-spectrum: 29 items) to being present in >50% of subjects ("affinities" with schizophrenia spectrum: 7 items). As predicted, EASE and CDS scores were correlated ($r=0.756$, 95% CI 0.665-0.840). These results show that ASE can be prevalent in Panic Disorder, including disturbances of self-awareness, body experience, and thought. Panic Disorder patients showed many common forms of derealization and depersonalization—perhaps involving more "secondary" and defensive psychological processes. They tended however to lack indicators suggesting truly profound distortion of the normal "transcendental" conditions of consciousness (i.e., as concerning the very constitution of subjective life or "basic self") that might constitute a more "primary" factor in schizophrenia, namely: 1) profoundly diminished sense of self-presence: 2) loss of the sense of existing as an independent entity (e.g., involving "confusion with the other") 3) solipsistic experiences of being the center of the universe, and 4) extreme reifications of subjective life). In this sense PD subjects appear similar to subjects with Depersonalization

Disorder or engaged in Introspection. Overall, the findings support the ipseity-disturbance or basic-self disturbance model of schizophrenia, while also indicating the need for careful phenomenological exploration of self-anomalies in order to distinguish transnosological "psychotic-like phenomena" from those of true psychotic or schizophrenic conditions.

2. Introduction

Anomalous self experiences (ASEs), presumably involving alterations in "core" or "minimal self," have been intensively studied in recent years—primarily as manifest in the schizophrenia spectrum, and as set in contrast with affective psychoses (especially bipolar) or psychopathology in general. The present study is the first to examine ASEs in Panic Disorder. The chief purpose is to begin exploring anomalous self-experience in the realm of anxiety disorders, and to further the knowledge of panic disorder in particular. An ancillary purpose is to help clarify precisely what might, or might not, be specific to the schizophrenia domain—which, in turn, could be useful for developing pathogenetic models for various disorders.

We will particularly emphasize depersonalization/derealization (d&d) experiences. These phenomena, which figure prominently among the ASEs, have long been recognized as common in psychosis and especially schizophrenia(Bleuler 1950),(Kraepelin & Lange 1927),(Berze & Gruhle 1929). Yet d&d experiences are found in several disorders, with chronic d&d having high prevalence(Aderibigbe et al. 2001) and with anxiety-inducing and traumatic situations serving as important triggers to these forms of what one author has termed "loss of the self"(Simeon & Abugel 2008).

Clinical research on ASE has primarily been conducted with the EASE: Examination of Anomalous Self Experiences, a semi-structured interview that operationalizes these anomalous experiences with a checklist of qualitative features(Parnas, Møller, et al. 2005),(Møller et al. 2011). Many EASE items clearly involve experiences that correspond to classic conceptions of depersonalization and derealization (see further in the CDS interview on Procedure section). Yet there is a particular relevance of Anomalous Self Experiences (ASEs) that has been conceptually(Sass & Parnas 2003; Kircher & David 2003), clinically(Raballo et al. 2011), and neurobiologically substantiated(Nelson et al. 2009; Kapur 2014),(Kircher & David 2003),(Taylor 2011). Moreover EASE research has identified ASEs in schizophrenia(Parnas, Møller, et al. 2005), in persons with schizotypic and schizotaxic traits(Raballo & Parnas 2011), in first-episode psychosis(Møller et al. 2011; Sass 2014), and in prodromal phases (Nelson et al. 2012),(Parnas et al. 1998),(Klosterkötter et al. 2001),(Nelson et al. 2009) . ASEs have also been shown to be quite rare both in other

functional psychoses(Parnas 2005);(Parnas et al. 2003);(Parnas, Handest, et al. 2005) and in a general personality-disorder sample(Nelson, A. Thompson, Chanen, et al. 2013).

It should be noted that EASE interviews focus on enduring or trait-like features rather than on experiences that occur only during psychotic episodes(Parnas, Møller, et al. 2005) (or in the case of the PD sample, panic episodes). Given their apparent trait-like nature, such anomalies (which involve an altered sense of engagement or attunement to oneself and the world) hold promise for identifying those at ultra-high risk (Nelson et al. 2009);(Nelson et al. 2012) or schizophrenia-prone individuals (Nelson, A. Thompson & Yung 2013);(Parnas 2005).

Some reservations do however remain regarding the use of ASEs as markers of psychosis risk or schizophrenia-spectrum disorder. One problem is the seeming overlap between ASE and depersonalization/derealization experiences—given that the latter experiences: 1) are the third most common psychopathological symptom (after anxiety and depressive mood) and occur in non-schizophrenic pathologies, including anxiety disorders, depressive disorders(Brauer et al. 1970), and Depersonalization Disorder itself(Simeon et al. 1997); 2) show phenomenological complexity(Simeon et al. 2008);(Simeon & Abugel 2008); and 3) can be conceptualized dimensionally, and may occur as normal adaptive reactions to anxiety-provoking situations or even as voluntary responses (e.g., in introspection or meditation(Sass, Pienkos & Nelson 2013)). All this suggests the need to explore the possibility of specific *patterns* of ASE in more phenomenological detail, and also to clarify their presence and nature in non-schizophrenic(Sass, Pienkos, Nelson, et al. 2013) and non-pathological as well as in schizophrenia-spectrum settings(Sass, Pienkos & Nelson 2013).

Previous publications ((Sass 2014);(Borda & Sass 2015; Sass & Borda 2015)), backed by some empirical and quasi-empirical ((Hunt 1976);(Sass, Pienkos & Nelson 2013; Sass, Pienkos, Nelson, et al. 2013)) and review of neurocognitive findings (especially(Sass & Borda 2015)), distinguishes more primary from more secondary forms of self-disorder—arguing that each form may be *necessary* (but not sufficient, taken alone) for the development of schizophrenia. The more secondary forms seem to involve consequential and especially defensive factors, and might be less distinctive of schizophrenia in particular; these secondary forms seem, in any case, to have close affinities with the dissociation or dissociation-like phenomena (including depersonalization/derealization) that occur in

Depersonalization Disorder and PTSD, or even with volitional or quasi-volitional forms of depersonalization characteristic of introspection or meditation.

The present arm investigates anomalous subjective self-experiences in Panic Disorder (PD) and compares these with matched Healthy Controls (HC). Consistent with past uses of the EASE, only EASE items that occurred *outside* acute episodes of Panic Attacks[1] were scored.

The hypotheses were that ASEs would occur in patients with Panic Disorder: a) at a significantly higher level than in normal controls; and b) though at a lower level, on average, than that found previously in schizophrenia subjects. The third hypothesis was c) that, given the overlap in symptoms (especially in domains 1, 2 and 3), the number of ASEs would be correlated with the number of general depersonalization experiences. In addition, we intended to explore the profile of specific *types* of ASEs in PD patients. This implies considering the five, officially designated EASE domains (specified below), but also—and perhaps more importantly—any possible patterns of *individual* EASE items and sub-items that might be revealed; and analyzing these latter in light of the above-mentioned primary/secondary distinction and other theoretical considerations. Consistent with previous studies on introspectionism (Sass, Pienkos & Nelson 2013) and depersonalization disorder(Sass, Pienkos, Nelson, et al. 2013), it was considered "affinities" and "discrepancies" in the *types of ASEs* found in the PD subjects in comparison with those found in schizophrenia-spectrum samples.

[1] Here it was strictly considered EASE stipulations that state, in the case of two items, that the ASE item should not be rated (in the case of Derealization (2.5)) "after" or (in case of Primary Self-Reference Phenomena (5.1)) "before" a "panic attack." Also, with one exception, sub-items under the item Anxiety (2.13) were only rated when they occurred *outside* Panic Attacks. The exception is Subtype 1: panic attacks with autonomic symptoms (2.13.1)—which by definition involve panic attacks and had to be present in the panic-disorder subjects.

3. Methods

3.1 Setting and sample

The sample included 47 subjects diagnosed with Panic Disorder (ICD-10) and active panic attacks, all from Santa Maria Hospital Psychiatric Outpatient Clinic (CHLN – North Lisbon Central Hospital). The PD patients were all referred to the CHLN hospital from Primary Care facilities and the Emergency Departments only after there had been no symptomatic response after 1-month treatment with Selective Serotonin Reuptake Inhibitors; this sample was therefore somewhat more severe (or at least recalcitrant to standard treatment) than average for PD patients. Our patients were referred to a hospital setting where they were given the diagnosis of Panic Disorder and no other diagnosis. Our sample was selected under the inclusion criteria of no physical or psychiatric co-morbidity at the time of diagnosis. After admission subjects underwent screening instruments and a multidisciplinary assessment (psychiatric and psychological). They were not given, at any time of follow-up, the diagnosis of any other disorder, such as Affective or Schizophrenic disorders.

PD subjects ranged from 20 to 75 years of age. 76% engaged in social drinking but none used alcohol on a regular basis. Although 85% of subjects had never used drugs, six subjects reported social cannabis consumption and one used this drug regularly. The psychopharmacological profile included antidepressants (93.61%), benzodiazepines (74.46%) and quetiapine (23%). On follow-up (average of 27 months; always greater than 12 months), the diagnosis remained Panic Disorder.

Control subjects were recruited via local advertisement requesting matching demographic features but absence of present or past personal or family psychiatric history. All subjects were recruited between August 2015 and December 2015; all signed a written voluntary informed consent form prior to participation. This study received ethical approval.

3.2 Socio-demographics

The Socio-demographic data included gender, age, country of birth, employment, education, present or past psychiatric treatment, and personal or family history of psychiatric disorder

(full-time students were considered employed). This information was gathered from the CHLN clinical file or, for control subjects, during research interviews.

The sample comprised 47 PD subjects with mean age of 38.17 years (SD 13.66) of which 31.9% were male. The matching sample of HC participants showed no differences on baseline demographics (see **Table 9)**, except that employment rates and education were higher in HC than PD (respectively, F 0.040 p=0.020 0.002 p=0.001*)—a point addressed below.

Table 9: Sociodemographic and Clinical Characterization of Sample

	Total sample (N=94) mean±SD or n (%)	HC (N=47) mean±SD or n (%)	PD (N=47) mean±SD or n (%)	F or Fisher's	p
Age at inclusion	38.63±15.13	39.09±16.61	38.17±13.656	0.085	p=0.771
Country of Birth				0.242	p=0.121
Portugal	38 (95)	47 (100)	44 (93.6)		
Other	2 (5)	0 (0)	3 (6.4)		
Gender				0.520	p=0.260
Male	34 (36.2)	19 (40.4)	15 (31.9)		
Female	60 (63.8)	28 (59.6)	32 (68.1)		
Ethnicity				1.000	p=0.692
Caucasian	90 (95.7)	45 (95.7)	45 (95.7)		
Other	4 (4.3)	2 (4.3)	2 (4.3)		
Employed/ Studying				0.040	p=0.020*
Yes	80 (85.1)	44 (93.6)	36 (23.4)		
No	14 (30)	3 (6.4)	11 (76.6)		
Education				0.002	p=0.001*
High-School	24 (25.5)	5 (10.6)	19 (40.4)		
Bachelor/Master degree	70 (74.5)	42 (89.4)	28 (59.6)		

number of subjects or Mean ± SD. Percentages under parenthesis. p-values refer to ANOVA between HC and PD groups for continuous and categorical values respectively. * Significant difference (2-tailed p<0.05)

3.3 Procedure

Patients in the study were administered the EASE: Examination of Anomalous Self Experiences (a semi-structured, qualitatively rich, clinical interview), the Social and

Occupational Functioning Assessment (SOFA), and the Cambridge Depersonalization Scale (CDS, a structured clinical interview).

Semi-structured interviews were always performed by two psychiatrists (LM and either SC or CC), who were blind to clinical diagnosis and had extensive training in psychopathology and a cthese in using the EASE. Scoring of 9 (out of 47) audio-recorded interviews, and joint discussion of difficulties and disparities, ensured inter-rater reliability. Also, in all cases where scoring proved problematic, EASE scores were assigned by consensus after joint discussion.

3.4 Clinical Measures

Social and Occupation Functioning Assessment Scale: SOFAS(Goldman et al. 1992)

This modified version of the Global Assessment of Functioning (GAF) scale attempts to measure social and occupational functioning independently of symptoms and psychological functioning. SOFA Scores were based on information obtained in clinical records and psychiatric interview, and could range from 0 to 100.

Examination of Anomalous Self Experiences checklist: EASE(Parnas, Møller, et al. 2005)

This semi-structured interview for unusual subjective experiences is intended to investigate anomalous experiences primarily involving the "pre-reflective" sense of first-person perspective or basic self(Møller et al. 2011)—a.k.a. as "minimal" or "core" self. It has been translated into various languages, including Portuguese by Nelson Goldenstein and his research group. Interrater reliability is good, with a Cronbach α of 0,87(Møller et al. 2011). The EASE has 57 items, divided into five subscales with a total of 94 items and sub-items: a) 28 cognition and stream of consciousness items; b) 36 self-awareness and presence items; c) 16 bodily experiences items; d) 6 demarcation/transitivism items; e) 8 existential reorientation items. As in previous EASE research, scoring was dichotomous, indicating presence (1) or absence (0) of items. The use of the EASE included the examination of items (and sub-items) found in schizophrenia that were found to be either quite common ("affinities") or quite rare ("discrepancies") in this PD sample.

It should be noted that the "discrepancies" referred to below in the paper were operationalized in two distinct ways. In the *previous* studies of Depersonalization Disorder Disorder(Sass, Pienkos, Nelson, et al. 2013) and Introspectionism(Sass, Pienkos & Nelson 2013) considered below, "discrepancy" referred to an EASE item that was not reported by any subject in the sample, and was therefore deemed "discrepant" with schizophrenia-spectrum results (on which the EASE in based). In the PD sample in *this* study, "discrepancies" were defined as items or sub-items that were reported by <10% of the sample subjects.

Since the previous vs current studies used different methods, they are not directly comparable. The two previous studies were quasi-empirical in nature: they did not employ actual EASE interviews, but, rather, applied EASE categories to previously published self-reports by persons with the conditions at issue. Subjects in those studies therefore had to mention EASE items *spontaneously* in their autobiographical accounts; individual EASE items were not systematically queried. The PD sample in the present study was thus more carefully probed for ASEs than in the prior Introspectionism(Sass, Pienkos & Nelson 2013) and Depersonalization-Disorder(Sass, Pienkos, Nelson, et al. 2013) studies.

Cambridge Depersonalization Scale, (CDS)(Sierra & Berrios 2000)

This 29-item self-report scale (Cronbach α of 0,89) measures the frequency and duration of depersonalization and derealization experiences. Frequency is rated from 0 (never) to 4 (all the time); duration from 1 (few seconds) to 6 (more than a week). It has been translated into Portuguese (also re-translated into English) and used in various research projects with Portuguese speakers. Comparison of EASE items with depersonalization/derealization items in the Cambridge Depersonalization Scale reveals two groups of d/d symptoms:

- 13 EASE items, all from Domains 1, 2, 3, were more or less *identical* with CDS items. These include: Discordance between expression and expressed (1.16); Disturbance of expressive language function (1.17); Distorted First Person Perspective Subtypes 1 and 2 (2.2.1 and 2.2.2); Melancholiform depersonalization (2.3.1); Diminished Presence Subtype 1 (2.4.1); Dissociative Depersonalization Subtype 1 and 2 (2.8.1 and 2.8.2); Morphological Change Subtypes 1 and 2 (3.1.1. and 3.1.2); Motor disturbances subtypes 1, 2 and 5 (3.8.1, 3.8.2 and 3.8.5).

- 11 EASE items, also from Domains 1, 2, 3, show a *close affinity* with CDS items. These include: Thought interference (1.1); Loss of thought ipseity (1.2); Disturbance of thought initiative/intentionality (1.11); Disturbance of time experience Subtype 1 (1.14.1); Psychic Depersonalization: unspecified (2.3.2); Diminished Presence: distance to the world (2.4.2); Diminished Presence: as subtype 2 plus derealization (2.4.3); Derealization: fluid global derealization (2.5.1); Diminished transparency of consciousness (2.15); Somatic depersonalization (3.3); Psychophysical misfit / split (3.4).

3.5 Statistical Analysis

Descriptive statistics, including t-tests for continuous variables and Fisher's or Pearson chi^2 for categorical variables, were used to consider between-group differences. Non-parametric tests were employed when the assumptions for parametric null hypothesis tests were violated.

As a first aim it was measured the prevalence of ASE using the EASE in PD and matched HC subjects, considering both overall and individual-domain scores. Since the normality- and homogeneity-of-variance assumptions for the SOFAS and EASE were violated, it was performed Mann-Whitney non-parametric tests to compare HC and PD samples. When not otherwise specified, two-tailed $p<0.05$ was considered significant. Given the exploratory nature of this small-sample study, it was decided not to control for family-wise error rate, which would have decreased statistical power. To compare mean EASE scores with other samples, scores from schizophrenia and bipolar samples were used (Nordgaard & Parnas 2014), (Raballo & Parnas 2012), (Haug, Lien, et al. 2012). Pearson r was used to analyze the correlation between the EASE and CDS scores in the sample. Standard descriptive statistics were employed to determine the ASE items percentage profile in the subjects. All analyses were performed using SPSS IBM 22.

Since previous studies considering depersonalization disorder (Sass, Pienkos, Nelson, et al. 2013) and introspectionism (Sass, Pienkos & Nelson 2013) were *quasi*-empirical, they do not allow for direct comparisons with these PD findings (as noted above, in these studies EASE categories were applied not to interviews but to previously published reports). They

do, however, allow for comparing items that seem to be especially *rare* outside schizophrenia — as explained below.

4. Results

4.1 Socio-demographic characterization

Interviews (EASE+CDS): took on average 1h16min (SD=0.31) in HC and 2h23 min (SD=0.39) in PD subjects.

4.2 Prevalence of ASE and average EASE scores

ASEs, as measured by the EASE, were present in all 47 of the PD subjects, with an average EASE score (mean ± SD) of 17.94±11.88, largely reflecting domains 1 and 2. Mean ASE scores of individual EASE domains were: 1) Cognition and Stream of thought: 6.53±4.4; 2) Self-experience: 8.68±6.02; 3) Bodily experiences: 1.32±2.11, 4) Demarcation/transitivism: 0.26±0.49; and 5) Existential reorientation: 0.70±1.317.

In the comparison sample of 47 HD subjects, ASEs occurred in 20 subjects; of these, 16 had scores below 5, with a maximum of 8 (in one subject). The average HD EASE score was 1.00±1.72.

We found a significant difference in EASE scores overall, as well as in each specific domain (somewhat surprisingly, given the lower scores for domains 4 and 5). **Table 10** presents' between-groups differences in EASE and SOFAS scores. **Figure 5** offers a boxplot representation of EASE overall score in HC and PD samples.

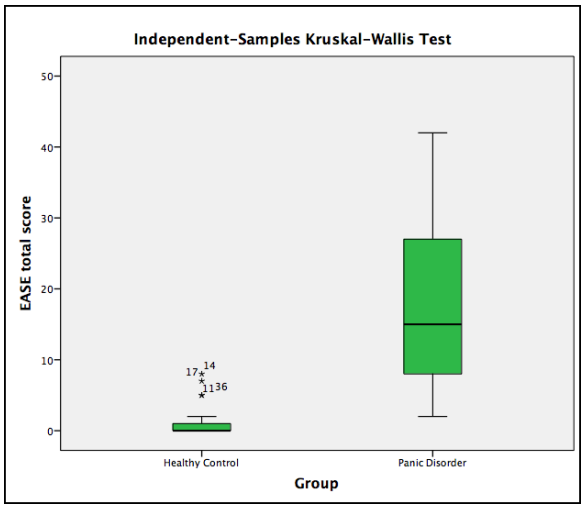
Table 10: Between groups differences in EASE and SOFAS scores

	HC (N=47) median (range) Mean rank	PD (N=47) median (range) Mean rank	U	p
CDS score	2.00 (0-27) 31.60	29.00 (0-110) 63.40	357.000	p<0.001
EASE score	0.00 (0-8) 24.89	15.00 (2-42) 70.11	42.000	p<0.001
EASE Cognition and Consciousness score	0.00 (0-8) 27.43	6.00 (0-16) 67.57	161.000	p<0.001
EASE Self-awareness and Presence domain	0.00 (0-5) 26.88	7.00 (0-22) 68.12	135.500	p<0.001
EASE Bodily experiences domain	0.00 (0-0) 37.50	0.00 (0-9) 57.50	634.500	p<0.001
EASE Demarcation/ transitivism domain	0.00 (0-0) 42.00	0.00 (0-2) 53.00	846.000	p<0.001
EASE Existential Reorientation score	0.00 (0-0) 40.50	0.50 (0-5) 54.50	775.500	p<0.001
SOFAS score	90 (90-100) 68.46	60.00 (40-75) 26.54	119.500	p<0.001

Two groups were compared and considering the non-normal distribution of data and heterogeneity of variance, the Mann-Whitney non-parametric test was adopted. Median (with range) and mean rank for each group are reported. P values correspond to differences between the two groups. Abbreviations: HC: Healthy controls; PD: Panic Disorder subjects

Figure 5: Distribution of EASE Scores in HC and Panic Disorder samples

The two groups differed for total EASE score (N=94, *H(2)=66.271, p<0.001*)

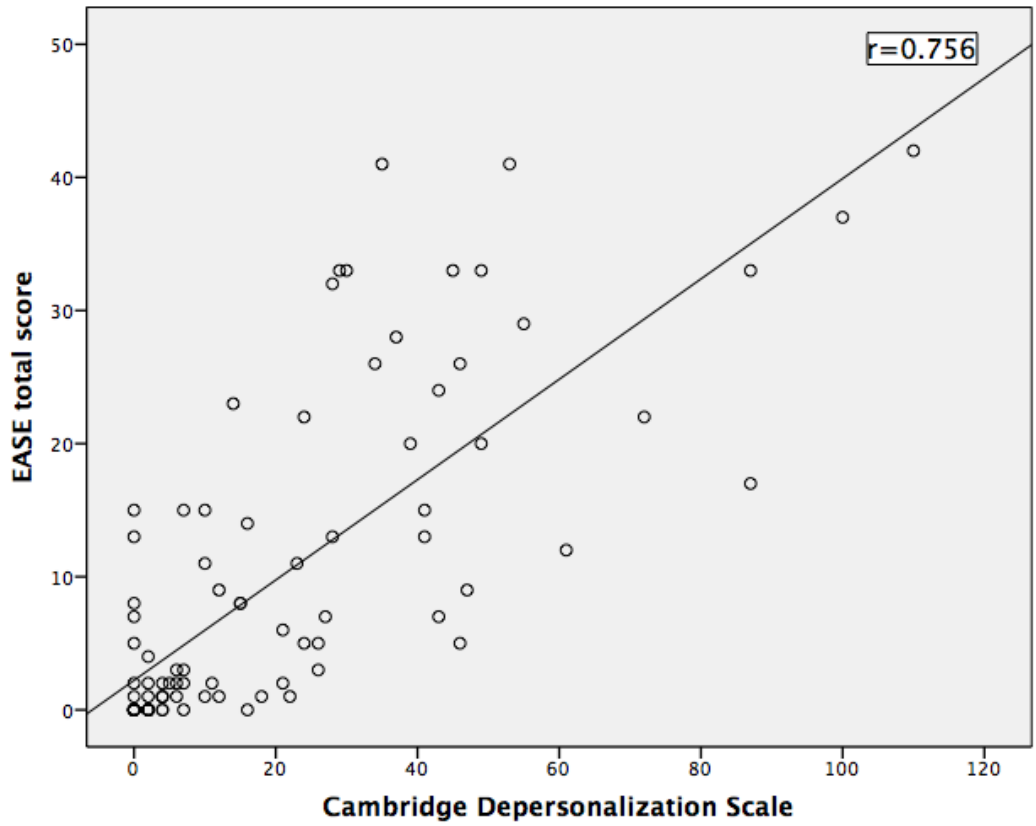


4.3 Correlation between EASE and CDS scores

Not surprisingly, it confirmed the prediction of a significant correlation between CDS depersonalization and derealization scores and overall EASE scores in the sample (see **Figure 6**), with Pearson r=0.756, 95% CI 0.665-0.840, p<0.001. Correlations of CDS scores with domains 1, 2 and 3 scores were especially high (respectively 0.736, 95% 0.637-0.835, p<0.001; 0.688, 95% 0.518-0.815, p<0.005; and 0.658 0.451-0.800, p<0.005).

Figure 6: Correlation between EASE and CDS score in the sample

(r=0.756, 95% CI 0.665-0.840, p<0.001 bootstrap method applied)



4.4 Distribution (percentages) of individual EASE sub-items in the PD sample

As shown in **Table 11**, certain EASE items or sub-items were especially common in the PD sample. The most frequently items (i.e., reported by >50% of PD subjects) were: Thought pressure (1.3), ruminations subtype 1 (1.6.1), Disturbance of time experience Subtype 1 and 2 (1.14.1 and 1.14.2); as well as (not surprisingly) assorted anxiety experiences including panic attacks with autonomous symptoms (2.13.1), psychic mental anxiety (2.13.2) phobic anxiety (2.13.3), and social anxiety (2.13.4).

Also of interest are "discrepancies"—namely, EASE items presumably found in schizophrenia-spectrum subjects but either absent or rare (<10%) in the panic-disorder sample. Only two EASE items were *never* reported by the PD subjects: namely, Perceptualization of inner speech: as external (1.7.4) and Sense of change in relation to gender: fear of being of the opposite sex (2.11.1). Also of interest are a considerable number of items and sub-items (32) that were *rarely* reported (<10% of the sample), for these may

suggest significant deviance from the schizophrenia-spectrum patients on which the EASE is based. They are presented in **Table 12,** which also shows, for comparative purposes, the "discrepancies" (vis a vis schizophrenia-spectrum) found in prior, quasi-empirical studies of Depersonalization Disorder and of Introspectionism (reminder: "discrepancy" refers to EASE items, presumably characteristic of schizophrenia, that were *not* found in published reports of the latter two conditions).

Table 11: Distribution of EASE items and sub-items according to their percentage across PD sample (47 subjects)

% of PD sample	Cognition and Stream of Consciousness domain	Self-Awareness domain	Bodily Experiences domain	Transitivism Domain	Existential domain
<10%	1.4.2 Thought fading; 1.4.3 Thought Combination; 1.5 Silent Thought Eco; 1.8 Spatialization of experience; 1.7.2 1.7.3 1.7.4: perceptualization of inner speech: equivalents and internal as first rank symptoms and as external 1.10 Inability to discriminate modalities of intentionality 1.11 Disturbance of thought initiative;	2.1.2 Diminished sense of basic Self from adolescence; 2.2.3 Spatialization of the self; 2.7.1 2.7.3 I-split: as if and as a spatialized experience; 2.11.1 Fear of being of the opposite sex; 2.18.2 diminished vitality trait like;	3.1.1 3.1.2 Sensation and Perception of change 3.2.3 Mirror related: other; 3.4 Psychophysical Misfit / Split; 3.5 body disintegration; 3.6 Spatialization of bodily experiences; 3.8.1 3.8.2 3.8.3 3.8.4 Pseudo-movements and motor interference motor blocking and sense of motor paresis; 3.9 mimetic experience;	4.1 confusion with the other; 4.2 confusion with specular image; 4.3.2 feeling of fusion/disappearance with physical contact; 4.4 passivity mood; 4.5 Other transitivistic phenomena;	5.3 Feeling as if his experiential field is the only extant reality; 5.4 Feeling as if having an extraordinary creative power; 5.7 Existential or intellectual change;
10-20%	1.6.4 Pseudo-obsessions; 1.12.2 Inability to split attention;	2.1 Diminished sense of basic Self: early life; 2.2.1 Distorted mineness/selfhood; 2.4.2 Distance to the world 2.4.3 Diminished presence with derealization; 2.5.2 Intrusive derealization; 2.8.2 Dissociative visual hallucination; 2.10 Sense of change in Chronological age; 2.11.1 Fear of being homosexual; 2.12 loss of common sense;	3.2.1 3.2.2 Mirror-related search for change or perception of change; 3.7 Cenesthetic experiences; 3.8.5 desautomation of movement;	4.3.1 anxiety with physical contact;	5.1 Primary self-reference phenomena; 5.2 feeling of centrality; 5.6 magical ideas linked to the subjects way of experiencing; 5.8 Solipsistic grandiosity;
20-30%	1.2 Loss of Thought Ipseity; 1.6.2 Secondary Rumination; 1.9 Ambivalence; 1.12.1 Captivation by details;	2.2.2 Experiential distance in perspective; 2.4.1 Diminished presence: not being affected; 2.6 Hyperreflectivity; 2.7.1 I-split suspected; 2.9 Identity confusion; 2.15 diminished transparency of consciousness; 2.16 Diminished initiative;	3.3 Somatic depersonalization;		5.5 Feeling as if the world is not truly real;
30-40%	1.4.1 Thought blocking 1.6.5 Rituals/Compulsions; 1.7 Perceptualization of inner speech: internal, 1.13 Disorder of short term memory; 1.15 discontinuous awareness of action; 1.16 Discordance expression/expressed; 1.17 Disturbance of language;	2.3.1 2.3.2 Depersonalization; melancholiform and unspecified forms 2.14 ontological Anxiety; 2.17 hypohedonia			
40-50%	1.1 Thought Interference; 1.6.3 True obsessions;	2.5.1 Fluid global derealization; 2.8.1 Dissociative depersonalization: “as if”; 2.13.5 Diffuse free floating anxiety; 2.18.1 diminished vitality state like; 2.13.3 phobic anxiety; 2.13.6 paranoid anxiety			
>50%	1.3 Thought Pressure; 1.6.1 Pure Rumination; 1.14.1 disturbance in subjective time; 1.14.2 disturbance in existential time;	2.13.1 Panic Attacks with autonomic symptoms; 2.13.2 Psychic mental anxiety; 2.13.4 Social Anxiety;			

Table 12: "Discrepancies" in the EASE in Depersonalization, Introspectionism and Panic Disorder versus Schizophrenic spectrum disorders

Depersonalization discrepancy (absence)*	Introspectionism discrepancy (absence)*	Panic Disorder discrepancy (<10%)*
1.1 Thought interference; 1.5 Silent Thought Echo; 1.13 Disorder of short-term memory; 2.10 Sense of change in chronological age; 2.11 Sense of change in gender; 3.9 Mimetic experience 4.1 Confusion with the other; 4.2 Confusion with own specular image; 5.1 Primary self-reference phenomena; 5.2 Feelings of centrality; 5.3; Feeling as if experiential field is only extant reality; 5.6 Magical ideas; 5.8 Solipsistic grandiosity	1.16 Discordance between intended expression and the expressed; 1.17 Disturbance of expressive language function; 2.9 Identity confusion; 2.10 Sense of change in relation to chronological age; 2.11 gender; 2.18 diminished vitality; 3.5 Bodily disintegration; 3.9 and Mimetic experience; 4.3.2 feeling of fusion/disappearance with physical contact; 5.7 existential change and 5.8 solipsistic grandiosity	1.4.2 Thought fading; 1.4.3 Thought Combination; 1.5 Silent Thought Eco; 1.8 Spatialization of experience; 1.7.2 1.7.3 1.7.4: perceptualization of inner speech: equivalents and internal as first rank symptoms and as external 1.10 Inability to discriminate modalities of intentionality 1.11 Disturbance of thought initiative; 2.1.2 Diminished sense of basic Self from adolescence; 2.2.3 Spatialization of the self; 2.7.1 2.7.3 I-split: as if and as a spatialized experience; 2.11.1 Fear of being of the opposite sex; 2.18.2 diminished vitality trait like; 3.1.1 3.1.2 Sensation and Perception of change 3.2.3 Mirror related: other; 3.4 Psychophysical Misfit / Split; 3.5 body disintegration; 3.6 Spatialization of bodily experiences; 3.8.1 3.8.2 3.8.3 3.8.4 Pseudo-movements and motor interference motor blocking and sense of motor paresis; 3.9 mimetic experience; 4.1 confusion with the other; 4.2 confusion with specular image; 4.3.2 feeling of fusion/disappearance with physical contact; 4.4 passivity mood; 4.5 Other transitivistic phenomena; 5.3 Feeling as if his experiential field is the only extant reality; 5.4 Feeling as if having an extraordinary creative power; 5.7 Existential or intellectual change;

* For Depersonalization and Introspectionism, "discrepancy" means – not reported at all; while for the (more extensively probed) Panic-Disorder sample, it means – <10% of subjects reported the item. The items presented for Depersonalization Disorder and for Introspectionism are from (Sass, Pienkos, Nelson, et al. 2013) and from (Sass, Pienkos & Nelson 2013), respectively.

5. Discussion

This is the first empirical investigation of ASE in Panic Disorder. The chief aim was to determine whether ASEs — previously reported mostly in schizophrenia-spectrum patients — were present in significant amounts in PD subjects vs in matched controls. Also of interest are the possible *differences* between the ASE profiles of PD versus schizophrenia spectrum.

5.1 ASEs prominent in Panic Disorder subjects (affinities):

Overall EASE scores were, in fact, much higher in the PD group than in the normal (HC) sample, with a significant difference also for each of the five EASE domains. This mainly reflects high scores in the first three domains. It is noteworthy, however, that although scores on "demarcation/transitivism" and "Existential Reorientation" were quite low, they too were significantly different from HC.

As noted, 27 healthy-control subjects (HC) reported *no* ASE experiences (vs zero for the PD sample). Of the 20 HC subjects who did report some ASE, 16 had scores of 4 or less (4 subjects had scores between 5-8) — a finding consistent with previously studied samples(Sass 2014; Nelson, A. Thompson & Yung 2013; Raballo et al. 2011)). It is noteworthy that comparable previous research studies (using a standardized EASE technique) showed an average EASE score in schizophrenia-spectrum patients of 25.3 (Haug, Melle, et al. 2012), 21.4 (Raballo & Parnas 2012) and 19.6 (Nordgaard & Parnas 2014), $p<0.05$. The PD scores—average score of 17.94±11.88 — are somewhat lower than these, but considerably higher than those reported for bipolar psychosis (average of 6.3, $p<0.05$) and other mental disorders (average of 8.1, $p<0.05$) in the just-cited comparative studies.

If replicated, the finding that ASEs can be prominent in anxiety and in Panic Disorder, outside actual Panic Attacks, has significant psychopathological implications. Though the subjects' ASEs could be argued to be secondary to their Panic Attacks, they seem generally to reflect longer-term features of personality. The EASE interview does require that the items considered positive be pervasive, continuous and relevant to subjects ongoing well-being. Indeed, it is quite possible that ASEs might play a role in *creating* the anxious situations or orientation in which Panic Attacks could ensue. It is noteworthy that a number of PD subjects did describe their ASE experiences as lifelong but it is also significant that some of such patients felt they had had panic attacks since early in life, long before they were diagnosed.

As noted in Table 3, thought Pressure (1.3), pure Rumination (1.6.1), and disturbance of time experience in subjective time (1.14.1) as well as in existential time (1.14.2) were all highly common in PD subjects (>50%). The first two experiences are already considered in the standard anamnesis of anxiety. The findings suggest that altered time experience might be another key aspect of subjectivity –of much disregarded set of phenomena in need of being studied(Nordgaard et al. 2013). And as noted, the EASE findings regarding thought process and self-experience show that panic-disorder patients can often experience persistent and longstanding changes in thought process and assorted dissociative, de-realization and depersonalization experiences.

Not surprisingly, given the above-mentioned overlapping of items, high correlation between the EASE and CDS was found in this PD sample—a result consistent with finding frequent

derealization and depersonalization experiences in a previous UHR sample(Madeira, Bonoldi, Rocchetti, Brandizzi, et al. 2016).

Regarding the finding of significant levels of ASE in the panic disorder subjects, at least three possibilities must be considered (1) ASE in PD and in schizophrenia-spectrum might be the *same* phenomena, with severe anxiety the common denominator; (2) ASE in PD and schizophrenia-spectrum might be only superficially similar, though the EASE interview is unable to distinguish them; (3) somewhat different clusters of ASE might occur in schizophrenia-spectrum vs in Panic Disorder, such that close examination of EASE findings might be able to identify these distinct patterns.

We now consider the rarity of certain ASEs in panic disorder, a finding that would seem supportive of the third possibility.

5.2 ASEs rare in Panic Disorder (discrepancies):

Close examination of individual EASE items in this PD sample does allow us to identify some distinctive features of the panic-disorder ASE profile, for there are certain ASEs—presumably characteristic of schizophrenia-spectrum—that seem absent or rare (<10% of the subjects) in PD. These rare or absent ASEs can be grouped and labeled as follows:

1) A profoundly diminished sense of self-presence: “diminished sense of basic Self from adolescence” (2.1.2), “loss of first Person Perspective” (2.2), “diminished vitality trait-like” (item 2.18.2),

2) A loss of the sense of existing as an independent entity: “confusion with the other” (4.1) and “feelings of fusion” (4.3).

3) Solipsistic experiences of being the center of the universe: “feeling that the experiential field is only reality” (5.3)

4) Extreme reifications of subjective life: spatialization of experience (1.8), spatialization of self (2.2.3), “I-split as a spatialized experience” (2.7.3), Spatialization of bodily experiences (3.6); and Perceptualization of inner speech: equivalents, internal as first rank symptom and external (1.7.2, 1.7.3 and 1.7.4, the latter is 0%).

All these items (rarely reported in the PD sample) would seem to suggest a profound distortion of the normal "transcendental" conditions of consciousness (in a Kantian sense—i.e., as concerning the very constitution of subjective life). It has been suggested that they may be related, on the neurobiological plane, to forms of basic perceptual dys-integration that have been found in persons prone to schizophrenia—forms involving a failure to synthesize different *modalities* of perception, especially exteroceptive and interoceptive(Borda & Sass 2015). By contrast, the anomalous self experiences commonly found in PD would be largely of a different kind, probably involving more "secondary" and defensive phenomena including more standard forms of depersonalization and derealization(Sass & Borda 2015).

In this light, it is worth noting the rarity, even in severe Panic Disorder, of items in the Existential-Reorientation domain that would suggest one of the following: major changes of general metaphysical perspective (item 5.7), quasi-solipsistic views regarding one's own unusual creative powers (item 5.4) or one's status as the center of existence (item 5.2), or the sense that one's experiential field is the only extant reality (item 5.3). The rarity of these items suggests that even severe PD patients are unlikely to depart radically from standard metaphysical assumptions or a shared inter-subjective orientation, perhaps reflecting a less extreme alteration of the most basic coordinates of experience.

A final set of items rare in the PD sample is somewhat more difficult to interpret. These items, apparently associated with some formal disorder of thought process, are "thought fading" (1.4.2), "thought combination" (1.4.3), and "disturbance of thought initiative" (1.11). Their scarcity in the subjects suggest that thought process in anxious subjects does *not* typically manifest the kind of weakening or blurring, of initiative or clarity of theme, suggested by these items. Yet by contrast, "thought interference" (item 1.1: >40%) and "thought blocking" (sub-item 1.4.1: >30%) were quite common; these latter may reflect a more choppy quality to the flow of thought in panic patients, perhaps involving *invasions by* unwanted thoughts and also *evasions of* needed thoughts. Though speculative, it is possible that closer qualitative examination of patient reports might reveal differences between panic-related halting or block of thinking versus what seems a more extreme blocking and perplexity characteristic of schizophrenia ("suddenly my head became empty when speaking or thinking," said one such patient, "I was lost and could not go back").

The resemblances of the results to "discrepancies" previously identified in Depersonalization Disorder and Introspectionism seem particularly noteworthy. As can be seen in **Table 4**, items rarest in the PD group, including indications of fusion and of solipsistic centrality, also tended to be absent in these previous studies of non-schizophrenia-spectrum subjects. Together these results suggest that, while schizophrenia might entail deeply grounded disturbance of the self (perhaps involving perceptual dysintegration, at the pre-reflective level of self-experience) or a longer-term dys-social orientation, such abnormalities tend to be less prominent, or even absent, in Panic Disorder, Depersonalization Disorder, and Introspectionism. The ASEs that *are* present suggest a depersonalization/derealization syndrome that might be more secondary or defensive in a pathogenetic sense(Sass & Borda 2015).

Overall, the findings support the ipseity-disturbance or basic-self disturbance model of schizophrenia(Sass & Parnas 2003), while also indicating the need for careful phenomenological exploration of possible types or qualities of self-anomalies in order to distinguish trans-nosological "psychotic-like phenomena" from those of true psychotic or schizophrenic conditions.

It is striking, nevertheless, that, though rare (<10%), most of the more severe ASEs were not entirely absent from the PD sample. It is difficult to know how to interpret this finding. One possibility is that there can be an occasional potential, within Panic Disorder itself, for some quite severe disruptions of the transcendental conditions or fundamental constitution of the self or the self/world relationship—disruptions that might sometimes be indistinguishable from schizophrenia. Still another explanation might postulate the presence, in some PD subjects, of subclinical schizotypal or other psychosis-prone traits that were not detected in the screening process; the severe nature of the PD patients—a sample being treated in a hospital setting – might make this more likely. A third possibility is that here there is a form of error variance that is perhaps inherent in any interviewing technique that elicits verbal reports intended to target such subtle levels of subjective life. These possibilities should all be considered in discussing the remaining, miscellaneous ASEs found in this sample.

5.3 ASEs with mid-range distribution in Panic Disorder:

The presence of the remaining ASEs in percentages ranging from 10-50% (see **Table 11**) do suggest that disturbances in subjectivity in persons prone to "Panic attacks" may be more heterogeneous, and potentially severe, than previously assumed. Question remains on the nature of this heterogeneity and its clinical implications. First, and along with the presence of more severe ASE, it is possible that diverse personality traits in the PD subjects might account for their differences in respect to ASE (e.g. subjects with schizoid and schizotypal traits would have higher ASE). It could also be considered that these represent patients also constitute unrecognized UHR subjects and that time will reveal a different diagnosis (e.g. schizophrenia). Indeed, both might help to explain why the patients were unresponsive to their initial psychopharmacological treatment (at least one-month trial of SSRIs—standard in Portugal), and were referred to a hospital setting, sometimes including use of anti-psychotics (e.g. quetiapine in 23% of patients). Perhaps an inquiry into ASE in the initial evaluation could have predicted their unresponsiveness to standardized treatment and their need for a tailored approach.

But also, the prominence of depersonalization/derealization phenomena in both PD and schizophrenia spectrum seems clear indicating the need for a careful phenomenological exploration of possible differences between the types or quality of (1) self anomalies especially characteristic of or specific to schizophrenia (e.g. extreme or "bizarre" phenomena affecting the fundamental structure of consciousness in its relationship to its world) versus (2) more widespread, unspecified depersonalization and derealization experiences. Such research could be relevant to refining the ASE for assessing factors for psychosis (and schizophrenia) in vulnerable adolescents. More generally, it might help distinguish psychotic-like experiences in the general population from those more characteristic of true psychotic conditions.

6. Limitations

The sample came from a single psychiatric clinic (CHLN) with specific selection processes and criteria; all the PD patients were hospitalized, indicating severe presentation of anxiety or recalcitrance to the standard treatment. This, together with the small sample size. limits the generalizability of the results. Also, despite the absence of personality-disorder

diagnoses in the clinical records, it is not possible to exclude that some of the subjects might have traits of schizoid/schizotypal personality disorders (see discussion).

Specific limitations include the significant differences in employment rates and in level of education across the HC and PD samples. The first discrepancy reflects the process of selection of the HC group, which was by advertisement in a hospital, with recruited subjects necessarily being "working staff". The second seems also artefactual, given that PD subjects were hospitalized patients, which is generally associated with a lower level of functioning. Lastly, the small sample size did not allow for determining the effect of drugs and alcohol in the overall scores.

7. Partial Synthesis

To the knowledge, this is the first study to explore prevalence and implications of ASE in subjects with PD. All the PD subjects (a hospitalized sample) did report ASEs with an average score considerably higher than previously found in bipolar psychosis and other (non-schizophrenic) mental disorders, but lower than in schizophrenia-spectrum samples. Together with finding a significant correlation between EASE and CDS scores, this suggests the need to further explore the differences as well as similarities between ASE associated with psychosis or schizophrenia and the depersonalization and derealization experiences more broadly found. The detailed probing of ASE revealed both "affinities" and "discrepancies" between the PD profile and that of schizophrenia. This, considered together with similar findings in studies of depersonalization and introspectionism samples, suggests that future research on self-disorders might attempt to identify specific sets more differentiating of schizophrenia (perhaps a "schizophrenic spectrum disorders cluster"). The study also furthers the knowledge of subjective phenomena characteristic of anxiety disorders. All this might help to improve diagnostic identification, prognostic prediction, and pathogenetic modeling in both anxiety disorders and schizophrenia spectrum. Future prospective and large-sample studies would be necessary to confirm the initial findings and speculations.

Chapter 5: General Discussion and Conclusions

1. General Discussion

This thesis is part of the current phenomenological effort to retrieve meaning of subjective experiences in the landscapes of diagnosis, treatment of Schizophrenia and Anxiety disorders. Since the DSM-III the search for reliability has favored objective symptoms and operational categories stipulating a simplistic approach to the complexity of human experience and grounding various validity claims (Insel 2009; Kendall 2011; Naber & Lambert 2009; Parnas et al. 2013; Tandon 2014; Tyrer & Kendall 2009) and rendering a psychopathology and a nosology with severe limitations. More particularly, the thesis is set on the problematic topic of finding the core of schizophrenia – today a heterogeneous category built up by various consensuses (Andreasen 2006; de Leon 2013; Kendler 2009; Stanghellini & Fusar-Poli 2012) and with great variation in presenting symptoms and course of illness (Silveira et al. 2012; Silverstein et al. 2014; Tandon et al. 2009; Tandon 2014). It is here that the paradigm of anomalous self-experiences (ASE) can be drawn from seminal contributions ((Conrad 1997),(Jaspers 1963)) and also up-to-date clinical (e.g. (Parnas, Moller, et al. 2005; Parnas, Handest, et al. 2005; Sass et al. 2011)) and translational studies (e.g. (Borda & Sass 2015; Sass & Borda 2015; Hur et al. 2014)). The nature of basic-self disturbances as "traits" grounded the model beyond the occurrence in patients with psychosis and schizophrenia into their presence in prodromal and Ultra-High-Risk Subjects (e.g. (Brent et al. 2014; Nelson et al. 2008; Nelson et al. 2012)). Indeed, and after these developments, new clusters of symptoms have emerged and are being tested as markers of psychosis such as the Truman Symptoms (Fusar-Poli, Howes, et al. 2008) and Abnormal bodily Experiences (Stanghellini et al. 2012).

Yet the general introduction of these new clinical components (including its addition to the psychopathological examination) benefits from more studies (Sass, Pienkos, Nelson, et al. 2013) on the phenomenological bearing of these experiences. This constitutes the particular of this thesis which probes the boundaries of anomalous self-experiences in UHR subjects and anxiety disorders (particularly Panic Disorder). First, it takes the new concept of "Truman Symptoms" as a new way of rendering ASE in UHR. Secondly, it further details the subset of bodily ASE in UHR subjects by the use of a new Questionnaire of Anomalous Bodily Phenomena (ABPq). Lastly, it examines basic-self disorders in Panic Disorder both

illuminating the (yet) mysterious phenomenology of subjective experience in anxious disorders and to further substantiate the possibility of clusters of ASE, some with greater bearing for schizophrenia spectrum patients while others accompany anxious settings.

The first arm of this thesis rendered the prevalence and specifity of TS in a UHR sample suggesting that they might be a phenotypic marker of this state. It raised the argument that TS might be a UHR "symptom" and a protagonist in identifying a subgroup of UHR subjects that have higher psychopathology. It also showed there was no relation between basic-self disturbances or Depersonalization scores and Truman symptoms – yet was speculated that it might represent a false negative due to the small sample size. The findings of a high correlation between Cambridge Depersonalization Scale and Examination of Anomalous Self Experiences add up to the the sharp need of segregating "basic self-disturbances" from unspecified depersonalization and derealization experiences. A full overlap would render narratives of general derealization and depersonalization experiences an important confounding factor to narratives suggesting disturbances of "basic-self" (and schizophrenia proneness).

On the arm on Abnormal Bodily Phenomena the UHR sample experienced Abnormal Bodily Phenomena, and half of the sample experiencing them prominently – raising the speculation that these might be phenotypic markers of psychosis vulnerability. Still, as much as 30% of the sample had no ABP fostering the heterogeneity of the HR states, which present various comorbidities and have diverse diagnostic and functional outcomes. Indeed, it suggested that the ABP questionnaire might assess phenomena unlike other criteria defining HR for psychosis (including bodily phenomena considered in the CAARMS). The presence of prominent ABP did not differentiate the HR sample across PANSS and SOFAS scores and that proABP subjects had lower CAARMS overall score. These results could respond for a weak statistical power due to small group size in each group and further studies with larger samples are need to clarify this issue. In this sample it was found that subjects referring prominent ABP did not have significantly higher EASE scores.

Lastly, the findings in the sample of Panic Disorder subjects demonstrated that they experience basic-self disturbances and that their scores are considerably higher than those reported for bipolar psychosis and other mental disorders in the comparative studies. At least three possibilities were considered (1) ASE in PD and in Schizophrenic Psychosis might be

the *same* phenomena, with severe anxiety the common denominator; (2) ASE in PD and schizophrenic psychosis might be only superficially similar, though the EASE interview is unable to distinguish them; (3) somewhat different clusters of ASE might occur in schizophrenic Psychosis vs Panic Disorder, such that close examination might be able to identify these distinct patterns. This research allowed the verification that many ASEs are rare (<10% of subjects) in Panic Disorder, particularly those that correspond to a profound distortion of subjective life related, on the neurobiological plane, to some forms of basic perceptual dys-integration that have been found in persons prone to schizophrenia. By contrast, the anomalous self experiences found in Panic Disorder could be largely of a different kind, probably involving more "secondary" and defensive phenomena and standard forms of depersonalization and derealization.

A major inference of the analysis of the PD sample are that greater detail into their phenomenology suggests the differentiation of specific expressions of anxiety that were, until today, concealed. It could be possible to speculate that such insight into traits and features of PD (to which Psychiatry was previously oblivious) could explain why the patients were unresponsive to their initial psychopharmacological treatment and were referred to a hospital setting. Indeed, the enquiry of ASE in their initial evaluation could have directly pointed their unresponsiveness to standardized treatment and their need for a tailored approach. Lastly, and along the results in the UHR sample, there was a high correlation between the ASE (EASE) and Depersonalization scores (CDS) in the PD sample. Given the overlapping of items this is not surprising and yet raises the need of carefully addressing their distinction at phenomenological level.

2. General Limitations

This study is limited by the small sample sizes to the point that two of its branches should be considered exploratory. This limitation together with the use of just two UHR clinics and the selection process should warn that these results could be false negatives or false positives. Other important limitations include the lack of follow up results and of a clinical control group (e.g. affective, anxious or personality disorders) both would help to better define the clinical relevance of TS and ABP in UHR and ASE in PD. Particularly (1) in the UHR sample – the conceptual and empirical heterogeneity of criteria can impair the use of the results and (2) in sample of Panic Disorder it is not possible to exclude traits of schizoid/schizotypal personality disorders which can tamper with the results (and comparison with schizophrenia samples). Lastly, use of prescribed drugs and of illicit substances was either not systematically appraised (UHR) or their effect cannot be determined due to small numbers (PD sample).

3. Conclusion and answers to research questions

3.1 Final Conclusion

Overall, these studies spread the understanding of anomalous self-experiences outside schizophrenia spectrum disorders studying their relevance as markers of risk of severe mental disorders and their possible status in anxiety disorders. First, that Truman Symptoms might occur in Ultra-High-Risk (UHR) subjects endorse the need of their enquiry and finding if they predict clinical outcomes. Possibly they display a contemporary way of formulating Anomalous Self Experiences (ASE) in UHR states. Second, Abnormal Bodily Phenomena might be a relevant psychopathological cluster in Ultra-High-Risk Subjects. Therefore, that a comprehensive phenomenological inquiry of this subset of ASE could be relevant to enrich the understanding of UHR states. Third, a cluster of "secondary" ASE emerged in subjects with Panic Disorder allowing the identification of new psychopathological particularities of this category. The results in Panic Disorder expose how these subjects lack more profound disturbances of basic self, which are present in schizophrenia. Notably, they illuminate the yet unmapped field of subjective phenomena, which might carry new meanings to the psychopathological examination.

All three branches of this thesis provided a critical appraisal of basic-self paradigm. Furthering the knowledge on the subjective experiences in anxious disorders and UHR, it provided insight into their subjective self-experiences and detail into the "disparities" and "affinities" that these subjects present vs schizophrenia. Fostering the specificity of ASE for schizophrenia spectrum disorders or identifying particular subsets is of key relevance for the use of this model in adolescence and Ultra-High-Risk subjects. Indeed in these situations, anxiety is very frequent and could account for psychotic-like experiences or derealisation and depersonalization experiences – similes of ASE and therefore a confounding element.

3.2 Answers to research questions

3.2.1 Question 1: Are TS present in subjects at Ultra High clinical risk for psychosis and are they a valid clinical construct with impact in UHR psychopathology?

TS were prevalent in in the UHR sample and were absent in matched HC's. The UHR subjects with TS had similar scores to the UHR without TS in the EASE, SOFAS, CDS, CAARMS, PANSS, with the exception of higher score on Existential Reorientation and Demarcation/transitivism EASE subscales and General Psychopathology PANSS subscale. Further studies are necessary to understand the impact on UHR psychopathology

3.2.2 Question 2: Is there a correlation between CDS and EASE scores?

In the UHR and Panic disorder samples the CDS and EASE scores were correlated. This is not surprising as many of the items in the CDS are more or less identical with EASE items, 13 by estimation, while others show a close affinity here, 11 estimated (though this involves matters of interpretation). A recent research track raised the worry that the constructs of derealisation and depersonalization and basic self-disturbances could overlap. This correlation carries a first hint into the need of a phenomenological exploration of possible types or qualities of self-anomalies in order to distinguish trans-nosological depersonalization and derealization phenomena from ASE of true psychotic or schizophrenic conditions.

3.2.3 Question 3: Are Abnormal Bodily Phenomena (ABP) present in a UHR sample and does their presence carry clinical implications?

ABP were highly prevalent (while absent from matched HC) and there were prominent ABP in 50% of Panic Disorder subjects. ABP could be a phenotypic component of HR psychopathology and particularly of a subgroup of these subjects. Future prospective, and with larger samples, studies are necessary before endorsing the considerations if ABP predicts clinical outcomes or treatment response in HR subjects.

3.2.4 Question 4: Are Anomalous Self-Experiences (ASE) present in a Panic Disorder (PD) sample and what are the "discrepancies" and "affinities" with schizophrenia scores?

All the PD subjects reported ASEs with an average score considerably higher than previously found non-schizophrenic samples. It supports the need to further explore the differences as well as similarities between ASE associated with psychosis or schizophrenia and the depersonalization and derealization experiences more broadly found. The detailed probing of ASE allowed the display of "affinities" and "discrepancies" between the PD profile and that of schizophrenia suggesting that there might be specific sets more differentiating of schizophrenia (perhaps a "schizophrenic spectrum disorders cluster"). The study also furthers the knowledge of subjective phenomena characteristic of anxiety disorders. All this might help to improve diagnostic identification, prognostic prediction, and pathogenetic modeling in both anxiety disorders and schizophrenia spectrum. Future prospective and large-sample studies would be necessary to confirm the initial findings and speculations.

References

Abeles, M., 1935. Psychogenic Loss of Personal Identity. *Archives of Neurology & Psychiatry*, 34(3), pp.587–604.

Addington, J. et al., 2015. North American Prodrome Longitudinal Study (NAPLS 2): The Prodromal Symptoms. In The Journal of nervous and mental disease. pp. 328–335.

Aderibigbe, Y.A., Bloch, R.M. & Walker, W.R., 2001. Prevalence of depersonalization and derealization experiences in a rural population. *Social psychiatry and psychiatric epidemiology*, 36(2), pp.63–69.

Alderman, T. et al., 2015. Negative symptoms and impaired social functioning predict later psychosis in Latino youth at clinical high risk in the North American prodromal longitudinal studies consortium. *Early intervention in psychiatry*, 9(6), pp.467–475.

Andreasen, N.C., 2006. DSM and the Death of Phenomenology in America: An Example of Unintended Consequences. *Schizophrenia bulletin*, 33(1), pp.108–112.

Association, A.P., 2013. *Diagnostic and Statistical Manual of Mental Disorders (DSM-5®)*, American Psychiatric Pub.

Baker, D. et al., 2003. Depersonalisation disorder: clinical features of 204 cases. *The British Journal of Psychiatry*, 182(5), pp.428–433.

Beike, D.R., Lampinen, J.M. & Behrend, D.A., 2004. *The Self and Memory*, Psychology Press.

Berze, J. & Gruhle, H.W., 1929. *Psychologie der Schizophrenie*, Berlin: Julius Springer.

Binswanger, L., 1957. *Schizophrenie*, Neske: Pfullingen.

Blankenburg, W., 1971. *La perte de l'évidence naturelle, contribution à la psychopathologie des schizophrénies pauvres en symptômes/Trad. par Jean-Michel Azorin et Tatoyan. ...*,

Bleuler, E., 1950. *Dementia praecox; or, The group of schizophrenias*, New York: International Universities Press.

Bleuler, E., 1924. *Textbook of Psychiatry*, London: George Alen & Unwin.

Borda, J.P. & Sass, L.A., 2015. Phenomenology and neurobiology of self disorder in schizophrenia: Primary factors. *Schizophrenia research*, 169(1-3), pp.464–473.

Bovet, P. & Parnas, J., 1993. Schizophrenic Delusions: A Phenomenological Approach. *Schizophrenia bulletin*, 19(3), pp.579–597.

Brauer, R., Harrow, M. & Tucker, G.J., 1970. Depersonalization phenomena in psychiatric patients. *The British journal of psychiatry : the journal of mental science*, 117(540), pp.509–515.

Brent, B.K. et al., 2014. Self-disturbances as a possible premorbid indicator of schizophrenia risk: A neurodevelopmental perspective. *Schizophrenia research*, 152(1), pp.73–80.

Broome, M.R. et al., 2005. Outreach and support in south London (OASIS): implementation of a clinical service for prodromal psychosis and the at risk mental state. *European psychiatry : the journal of the Association of European Psychiatrists*, 20(5-6), pp.372–378.

Bumke, O., 1936. *Lehrbuch der Geisteskrankheiten 4th Ed*, München: J.F. Bergmann-Verlag.

Carman, T. University of Arkansas Press, 1999. The Body in Husserl and Merleau-Ponty E. Minar, ed. *Philosophical Topics*, 27(2), pp.205–226.

Carr, V. et al., 2000. A risk factor screening and assessment protocol for schizophrenia and related psychosis. *The Australian and New Zealand journal of psychiatry*, 34((Suppl.)), pp.S170–S180.

Carrión, R.E. et al., 2013. Prediction of functional outcome in individuals at clinical high risk for psychosis. *JAMA psychiatry*, 70(11), pp.1133–1142.

Cermolacce, M., Naudin, J. & Parnas, J., 2007. The "minimal self" in psychopathology: Re-examining the self-disorders in the schizophrenia spectrum. *Consciousness and cognition*, 16(3), pp.703–714.

Clark, A., 2008. *Supersizing the Mind*, Oxford University Press.

Comparelli, A. et al., 2014. Basic symptoms and psychotic symptoms: their relationships in the at risk mental states, first episode and multi-episode schizophrenia. *Comprehensive psychiatry*, 55(4), pp.785–791.

Conrad, K., 2013. Beginning schizophrenia: attempt for a Gestalt-analysis of delusion. In Cambridge: Cambridge University Press, pp. 176–193.

Conrad, K., 1958. *Die beginnende Schizophrenie: Versuch einer Gestaltanalyse des Wahns*, Thieme Stuttgart.

Conrad, K., 1997. *La Esquizofrenia incipiente*, Madrid: Fundacion Archivos de Neurobiologia.

Correll, C.U. et al., 2014. The Bipolar Prodrome Symptom Interview and Scale-Prospective (BPSS-P): description and validation in a psychiatric sample and healthy controls. *Bipolar disorders*, 16(5), pp.505–522.

Csikszentmihalyi, M. & Csikszentmihalyi, I.S., 1992. *Optimal Experience*, Cambridge University Press.

Cutting, J., 1987. *The Clinical roots of the schizophrenia concept*, Cambridge University Press.

de Haan, S. & Fuchs, T., 2010. The ghost in the machine: disembodiment in

schizophrenia--two case studies. *Psychopathology*, 43(5), pp.327–333.

de Leon, J., 2013. Is Psychiatry Scientific? A Letter to a 21st Century Psychiatry Resident. *Psychiatry Investigation*, 10(3), p.205.

Dell, P.F. & O'Neil, J.A., 2010. *Dissociation and the Dissociative Disorders*, Routledge.

Dunn, O.J., 1964. Multiple comparisons using rank sums. *Technometrics*.

Dupré, E.P., 1925. *Pathologie de l''imagination et de l''émotivité*, Payot.

Ehrsson, H.H., Holmes, N.P. & Passingham, R.E., 2005. Touching a rubber hand: feeling of body ownership is associated with activity in multisensory brain areas. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 25(45), pp.10564–10573.

ELISA KRACKOW, 2010. Narratives distinguish experienced from imagined childhood events. *The American Journal of Psychology*, 123(1), p.71.

Erlenmeyer-Kimling, L. et al., 2000. Attention, Memory, and Motor Skills as Childhood Predictors of Schizophrenia-Related Psychoses: The New York High-Risk Project. *American Journal of Psychiatry*, 157(9), pp.1416–1422.

Ey, H., 1973. *Traite des Hallucinations (2 Vols.) Paris*, Masson.

Fava, G. et al., 2008. Prodromal Symptoms and Intermittent Drug Medication in Mood Disorders. *Pharmacopsychiatry*, 24(01), pp.28–30.

Figueira, M.L., 2015. The Subjectivity of the illness-experience. *Revista Portuguesa de Psiquiatria e Saúde Mental*, (1), pp.3–10.

Fis, N.P. et al., 2008. Executive dysfunction in Turkish children at high risk for schizophrenia. *European Child & Adolescent Psychiatry*, 17(7), pp.424–431.

Fish, F. J., Casey, P. R., & Kelly, B. 2006. Fish's Clinical Psychopathology. RCPsych Publications.

Fletcher, P.C. & Frith, C.D., 2008. Perceiving is believing: a Bayesian approach to explaining the positive symptoms of schizophrenia. *Nature Reviews Neuroscience*, 10(1), pp.48–58.

Frankl, V.E., 1975. *The Unconscious God*,

Fuchs, T., 2005a. Delusional mood and delusional perception -- a phenomenological analysis. *Psychopathology*, 38(3), pp.133–139.

Fuchs, T., 2005b. Implicit and Explicit Temporality. *Philosophy, Psychiatry, & Psychology*, 12(3), pp.195–198.

Fulford, D. et al., 2014. Symptom assessment in early psychosis: the use of well-established rating scales in clinical high-risk and recent-onset populations. *Psychiatry research*, 220(3), pp.1077–1083.

Fusar-Poli, P. & Meyer-Lindenberg, A., 2013a. Striatal presynaptic dopamine in schizophrenia, Part I: meta-analysis of dopamine active transporter (DAT) density. *Schizophrenia bulletin*, 39(1), pp.22–32.

Fusar-Poli, P. & Meyer-Lindenberg, A., 2013b. Striatal presynaptic dopamine in schizophrenia, part II: meta-analysis of [(18)F/(11)C]-DOPA PET studies. *Schizophrenia bulletin*, 39(1), pp.33–42.

Fusar-Poli, P. et al., 2015. Antidepressant, antipsychotic and psychological interventions in subjects at high clinical risk for psychosis: OASIS 6-year naturalistic study. *Psychological medicine*, 45(6), pp.1327–1339.

Fusar-Poli, P. et al., 2011. Neuroanatomy of vulnerability to psychosis: A voxel-based meta-analysis. *Neuroscience and biobehavioral reviews*, 35(5), pp.1175–1185.

Fusar-Poli, P. et al., 2007. Neurofunctional correlates of vulnerability to psychosis: A systematic review and meta-analysis. *Neuroscience and biobehavioral reviews*, 31(4), pp.465–484.

Fusar-Poli, P. et al., 2013. Outreach and support in south London (OASIS), 2001-2011: ten years of early diagnosis and treatment for young individuals at high clinical risk for psychosis. *European psychiatry : the journal of the Association of European Psychiatrists*, 28(5), pp.315–326.

Fusar-Poli, P. et al., 2010. Social dysfunction predicts two years clinical outcome in people at ultra high risk for psychosis. *Journal of psychiatric research*, 44(5), pp.294–301.

Fusar-Poli, P., Borgwardt, S. & Valmaggia, L., 2008. Heterogeneity in the Assessment of the At-Risk Mental State for Psychosis. *Psychiatric Services*, 59(7), pp.813–813.

Fusar-Poli, P., Deste, G., et al., 2012. Cognitive Functioning in Prodromal Psychosis. *Archives of general psychiatry*, 69(6), pp.562–571.

Fusar-Poli, P., Howes, O., et al., 2008. "Truman" signs and vulnerability to psychosis. *The British Journal of Psychiatry*, 193(2), pp.168–168.

Fusar-Poli, P., Nelson, B., et al., 2014. Comorbid depressive and anxiety disorders in 509 individuals with an at-risk mental state: impact on psychopathology and transition to psychosis. *Schizophrenia bulletin*, 40(1), pp.120–131.

Fusar-Poli, P., Radua, J., et al., 2012. Neuroanatomical maps of psychosis onset: voxel-wise meta-analysis of antipsychotic-naive VBM studies. *Schizophrenia bulletin*, 38(6), pp.1297–1307.

Fusar-Poli, P., Yung, A.R., et al., 2014. Lessons learned from the psychosis high-risk state: towards a general staging model of prodromal intervention. *Psychological medicine*, 44(1), pp.17–24.

Gallagher, I., 2000. Philosophical conceptions of the self: implications for cognitive science. *Trends in cognitive sciences*, 4(1), pp.14–21.

Gallagher, S., 2006. *How the Body Shapes the Mind*, Clarendon Press.

Gallagher, S., 2011. *The Oxford Handbook of the Self*, Oxford University Press.

Gallagher, S. & Cole, J., 2011. Dissociation in self-narrative. *Consciousness and cognition*, 20(1), pp.149–155.

Gallese, V. & Ferri, F., 2013. Jaspers, the body, and schizophrenia: the bodily self. *Psychopathology*, 46(5), pp.330–336.

Gallese, V. & Sinigaglia, C., 2010. The bodily self as power for action. *Neuropsychologia*, 48(3), pp.746–755.

Gamma, F. et al., 2014. Early Intermodal Integration in Offspring of Parents With Psychosis. *Schizophrenia bulletin*, 40(5), pp.992–1000.

Geertz, C., 1973. *The Interpretation of Cultures*, Basic Books.

Gibson, J.J., 2014. *The Ecological Approach to Visual Perception*, Psychology Press.

Gipps, R.G.T. & Fulford, K.W.M.B., 2004. Understanding the clinical concept of delusion: from an estranged to an engaged epistemology. *International review of psychiatry (Abingdon, England)*, 16(3), pp.225–235.

Goldman, H.H., Skodol, A.E. & Lave, T.R., 1992. Revising axis V for DSM-IV: a review of measures of social functioning. *American Journal of Psychiatry*, 149(9), pp.1148–1156.

Graham, G., 2014. *The Disordered Mind*, Routledge.

Griesinger, W., 1867. *Mental pathology and therapeutics*,

Gross, G., 1989. The "basic" symptoms of schizophrenia. *The British journal of psychiatry. Supplement*, (7), pp.21–5– discussion 37–40.

Gross, G. & Huber, G., 1985. Psychopathology of basic stages of schizophrenia in view of formal thought disturbances. *Psychopathology*, 18(2-3), pp.115–125.

Gross, G., Huber, G. & Klosterkötter, J., 1987. *Bonner Skala für die Beurteilung von Basissymptomen*, Berlin, Heidelberg, New York : Springer-Verlag.

Hanna, R. & Maiese, M., 2009. *Embodied Minds in Action*, OUP Oxford.

Haug, E., Lien, L., et al., 2012. Selective aggregation of self-disorders in first-treatment DSM-IV schizophrenia spectrum disorders. *The Journal of nervous and mental disease*, 200(7), pp.632–636.

Haug, E., Melle, I., et al., 2012. The association between anomalous self-experience and suicidality in first-episode schizophrenia seems mediated by depression. *Comprehensive psychiatry*, 53(5), pp.456–460.

Häfner, H. et al., 1998. The ABC Schizophrenia Study: a preliminary overview of the results. *Social psychiatry and psychiatric epidemiology*, 33(8), pp.380–386.

Häfner, H., Maurer, K. & an der Heiden, W., 2013. ABC Schizophrenia study: an

overview of results since 1996. *Social psychiatry and psychiatric epidemiology*, 48(7), pp.1021–1031.

Häfner, H., Riecher-Rössler, A., Hambrecht, M., et al., 1992. IRAOS: an instrument for the assessment of onset and early course of schizophrenia. *Schizophrenia research*, 6(3), pp.209–223.

Häfner, H., Riecher-Rössler, A., Maurer, K., et al., 1992. First onset and early symptomatology of schizophrenia. A chapter of epidemiological and neurobiological research into age and sex differences. *European archives of psychiatry and clinical neuroscience*, 242(2-3), pp.109–118.

Hemsley, D.R., 1976. Attention and information processing in schizophrenia. *The British journal of social and clinical psychology*, 15(2), pp.199–209.

Hemsley, D.R., 2005. The development of a cognitive model of schizophrenia: placing it in context. *Neuroscience and biobehavioral reviews*, 29(6), pp.977–988.

Hemsley, D.R., 1998. The disruption of the "sense of self" in schizophrenia: potential links with disturbances of information processing. *The British journal of medical psychology*, 71 (Pt 2), pp.115–124.

Herrera, G., Jordan, R. & Vera, L., 2006. Agency and Presence: A Common Dependence on Subjectivity? *Presence: Teleoperators and Virtual Environments*, 15(5), pp.539–552.

Hilgard, E.R., 1973. A neodissociation interpretation of pain reduction in hypnosis. *Psychological review*, 80(5), pp.396–411.

Holmes, E.A. et al., 2005. Are there two qualitatively distinct forms of dissociation? A review and some clinical implications. *Clinical psychology review*, 25(1), pp.1–23.

Howes, O.D. et al., 2007. Molecular imaging studies of the striatal dopaminergic system in psychosis and predictions for the prodromal phase of psychosis. *The British journal of psychiatry. Supplement*, 51(51), pp.s13–8.

Huber, G., 1985. *Negative or basic symptoms in schizophrenia and affective illness*, Biological psychiatry.

Huber, G. & Gross, G., 1989. The concept of basic symptoms in schizophrenic and schizoaffective psychoses. *Recenti progressi in medicina*, 80(12), pp.646–652.

Hunt, H.T., 1976. A Test of the Psychedelic Model of Altered States of Consciousness. *Archives of general psychiatry*, 33(7), pp.867–876.

Hur, J.-W. et al., 2014. The crisis of minimal self-awareness in schizophrenia: a meta-analytic review. *Schizophrenia research*, 152(1), pp.58–64.

Hutton, P. et al., 2011. Prevalence of violence risk factors in people at ultra-high risk of developing psychosis: a service audit. *Early intervention in psychiatry*, 6(1), pp.91–96.

Ilhan Yargiç, L. et al., 1998. Comparison of dissociative identity disorder with other

diagnostic groups using a structured interview in Turkey. *Comprehensive psychiatry*, 39(6), pp.345–351.

Insel, T.R., 2009. Translating Scientific Opportunity Into Public Health Impact. *Archives of general psychiatry*, 66(2), pp.128–133.

J Giuliano, A. et al., 2012. Neurocognition in the Psychosis Risk Syndrome: A Quantitative and Qualitative Review. *Current pharmaceutical design*, 18(4), pp.399–415.

Jackson, H.J., McGorry, P.D. & McKenzie, D., 1994. The reliability of DSM-III prodromal symptoms in first-episode psychotic patients. *Acta Psychiatrica Scandinavica*, 90(5), pp.375–378.

James, W., 1950. *The Principles of Psychology*, Courier Corporation.

Janet, P., 2015. *The Major Symptoms of Hysteria - Scholar's Choice Edition*,

Jardri, R. et al., 2013. The Neurodynamic Organization of Modality-Dependent Hallucinations. *Cerebral Cortex*, 23(5), pp.1108–1117.

Jaspers, K., 1963. *General Psychopathology 7th Ed*, Manchester: Manchester University Press.

Jaspers, K., 1997. *General Psychopathology*, John Hopkins University Press.

Jeannerod, M., 2003. The mechanism of self-recognition in humans. *Behavioural brain research*, 142(1-2), pp.1–15.

Jenner, F.A. & De Koning, A., Academic Press.

Kant, I., 2013. *Immanuel Kant's Critique Of Pure Reason*, Read Books Ltd.

Kapur, S., 2014. Psychosis as a State of Aberrant Salience: A Framework Linking Biology, Phenomenology, and Pharmacology in Schizophrenia. *American Journal of Psychiatry*, 160(1), pp.13–23.

Kapur, S., Mizrahi, R. & Li, M., 2005. From dopamine to salience to psychosis—linking biology, pharmacology and phenomenology of psychosis. *Schizophrenia research*, 79(1), pp.59–68.

Kato, S. & Ishiguro, T., 1997. Clinical courses of hypochondriac-cenesthopathic symptoms in schizophrenia. *Psychopathology*, 30(2), pp.76–82.

Kay, S.R., Fiszbein, A. & Opler, L.A., 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophrenia bulletin*, 13(2), pp.261–276.

Kendall, T., 2011. The rise and fall of the atypical antipsychotics. *The British journal of psychiatry : the journal of mental science*, 199(4), pp.266–268.

Kendler, K.S., 2009. An historical framework for psychiatric nosology. *Psychological medicine*, 39(12), pp.1935–1941.

Keshavan, M.S., DeLisi, L.E. & Seidman, L.J., 2011. Early and broadly defined psychosis risk mental states. *Schizophrenia research*, 126(1-3), pp.1–10.

Kircher, T. & David, A., 2003. *The Self in Neuroscience and Psychiatry*, Cambridge University Press.

Kircher, T. & David, A.S., 2009. Self-consciousness: an integrative approach from philosophy, psychopathology and the neurosciences. In T. Kircher & A. David, eds. *The Self in Neuroscience and Psychiatry*. Cambridge: Cambridge University Press, pp. 445–474.

Klosterkötter, J. et al., 2001. Diagnosing schizophrenia in the initial prodromal phase. *Archives of general psychiatry*, 58(2), pp.158–164.

Klosterkötter, J. et al., 2013. Prediction and prevention of schizophrenia: what has been achieved and where to go next? *World psychiatry : official journal of the World Psychiatric Association (WPA)*, 10(3), pp.165–174.

Kraepelin, E. & Lange, J., 1927. *Psychiatrie, 9th edn*, Leipzig: J A Barth.

Krüger, C. & Mace, C.J., 2010. Psychometric validation of the State Scale of Dissociation (SSD). *Psychology and Psychotherapy: Theory, Research and Practice*, 75(1), pp.33–51.

Krüger, H.-P., 2010. Persons and Their Bodies: The Körper/Leib Distinction and Helmuth Plessner's Theories of Ex-centric Positionality and Homo absconditus. *The Journal of Speculative Philosophy*, 24(3), pp.256–274.

Lallart, E., Lallart, X. & Jouvent, R., 2009. Agency, the sense of presence, and schizophrenia. *Cyberpsychology & behavior : the impact of the Internet, multimedia and virtual reality on behavior and society*, 12(2), pp.139–145.

Lee, T.Y. et al., 2014. Symptomatic and functional remission of subjects at clinical high risk for psychosis: A 2-year naturalistic observational study. *Schizophrenia research*, 156(2-3), pp.266–271.

Legrand, D., 2007. Pre-reflective self-as-subject from experiential and empirical perspectives. *Consciousness and cognition*, 16(3), pp.583–599.

Lencz, T. et al., 2004. Nonspecific and attenuated negative symptoms in patients at clinical high-risk for schizophrenia. *Schizophrenia research*, 68(1), pp.37–48.

Leong, S., Waits, W. & Diebold, C., 2006. Dissociative Amnesia and DSM-IV-TR Cluster C Personality Traits. *Psychiatry (Edgmont (Pa. : Township))*, 3(1), pp.51–55.

Lewin, K., 2013. *The Conceptual Representation and the Measurement of Psychological Forces*, Martino Fine Books.

Loewy, R.L. et al., 2005. The prodromal questionnaire (PQ): preliminary validation of a self-report screening measure for prodromal and psychotic syndromes. *Schizophrenia research*, 79(1), pp.117–125.

Lucchelli, F. & Spinnler, H., 2002. The "Psychogenic" Versus 'Organic' Conundrum of Pure Retrograde Amnesia: Is it Still Worth Pursuing? *Cortex; a journal devoted to the study of the nervous system and behavior*, 38(4), pp.665–669.

Ludwig, A.M., 1983. The psychobiological functions of dissociation. *American Journal of Clinical Hypnosis*, 26(2), pp.93–99.

Lynn, S.J. & Rhue, J.W., 1994. *Dissociation*, Guilford Press.

Lysaker, P.H. & Lysaker, J.T., 2008. *Schizophrenia and the fate of the self*, Oxford University Press, USA.

Lysaker, P.H. et al., 2005. Personal Narratives in Schizophrenia: Increases in Coherence Following 5 Months of Vocational Rehabilitation. *Psychiatric Rehabilitation Journal*, 29(1), pp.66–68.

Madeira, L., Bonoldi, I., Rocchetti, M., Brandizzi, M., et al., 2016. Prevalence and implications of Truman symptoms in subjects at ultra high risk for psychosis. *Psychiatry research*, 238, pp.270–276.

Madeira, L., Bonoldi, I., Rocchetti, M., Samson, C., et al., 2016. An initial investigation of abnormal bodily phenomena in subjects at ultra high risk for psychosis: Their prevalence and clinical implications. *Comprehensive psychiatry*, 66, pp.39–45.

Maiese, M., 2015a. *Embodied Selves and Divided Minds*, Oxford University Press.

Maiese, M., 2011. *Embodiment, Emotion, and Cognition*, London: Palgrave Macmillan UK.

Maiese, M., 2015b. Embodiment, Enactivism, and Affectivity. In *Embodied Selves and Divided Minds*. Oxford University Press, pp. 1–48.

Manoliu, A. et al., 2014. Aberrant dependence of default mode/central executive network interactions on anterior insular salience network activity in schizophrenia. *Schizophrenia bulletin*, 40(2), pp.428–437.

Martin, J.-R. & Pacherie, E., 2013. Out of nowhere: Thought insertion, ownership and context-integration. *Consciousness and cognition*, 22(1), pp.111–122.

Matussek, P., 1987. Studies in delusional perception. In *The Clinical roots of the schizophrenia concept*. CUP Archive.

Matussek, P., 1952. Studies on delusional perception. I. Changes of the perceived external world in incipient primary delusion. *Archiv für Psychiatrie und Nervenkrankheiten, Vereinigt mit Zeitschrift für die Gesamte Neurologie und Psychiatrie*, 189(4), p.279.

Mayer-Gross, W., 1932. Die Klinik der Schizophrenie

. In *Handbuch der Geisteskrankheiten Vol IX*. Berlin, Germany.

McGorry, P.D., 2015. Early Intervention in Psychosis. *The Journal of nervous and mental disease*, 203(5), pp.310–318.

McLean, K.C., Pasupathi, M. & Pals, J.L., 2007. Selves Creating Stories Creating Selves: A Process Model of Self-Development. *Personality and Social Psychology Review*, 11(3), pp.262–278.

Merleau-Ponty, M., 1962. *Phenomenology of Perception Routledge & Kegan Paul*, London.

Merleau-Ponty, M., 2013. *Phenomenology of Perception*, Routledge.

Miller, T.J. et al., 2003. Prodromal assessment with the structured interview for prodromal syndromes and the scale of prodromal symptoms: predictive validity, interrater reliability, and training to reliability. *Schizophrenia bulletin*, 29(4), pp.703–715.

Mishara, A.L., 2010. *Klaus Conrad (1905-1961): delusional mood, psychosis, and beginning schizophrenia.* 2009 ed.,

Mishara, A.L. & Fusar-Poli, P., 2013. The phenomenology and neurobiology of delusion formation during psychosis onset: Jaspers, Truman symptoms, and aberrant salience. *Schizophrenia bulletin*, 39(2), pp.278–286.

Monti, M.R. & Stanghellini, G., 1996. Psychopathology: An edgeless razor? *Comprehensive psychiatry*, 37(3), pp.196–204.

Moran, L.V. et al., 2013. Disruption of Anterior Insula Modulation of Large-Scale Brain Networks in Schizophrenia. *Biological psychiatry*, 74(6), pp.467–474.

Mula, M., Pini, S. & Cassano, G.B., 2007. The neurobiology and clinical significance of depersonalization in mood and anxiety disorders: a critical reappraisal. *Journal of affective disorders*, 99(1-3), pp.91–99.

Murray, C.J.L., 1996. The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020. In A. D. Lopez & C. J. L. Murray, eds. Cambridge, Massachusetts: Harvard School of Public Health, p. 43.

Murray, R.J., Schaer, M. & Debbané, M., 2012. Degrees of separation: A quantitative neuroimaging meta-analysis investigating self-specificity and shared neural activation between self- and other-reflection. *Neuroscience and biobehavioral reviews*, 36(3), pp.1043–1059.

Møller, P. et al., 2011. Examination of anomalous self-experience in first-episode psychosis: interrater reliability. *Psychopathology*, 44(6), pp.386–390.

Naber, D. & Lambert, M., 2009. The CATIE and CUtLASS Studies in Schizophrenia. *CNS Drugs*, PAP(8), pp.649–659.

Nekovarova, T. et al., 2014. Bridging disparate symptoms of schizophrenia: a triple network dysfunction theory. *Frontiers in Behavioral Neuroscience*, 8, p.19.

Nelson, B. et al., 2009. A disturbed sense of self in the psychosis prodrome: linking phenomenology and neurobiology. *Neuroscience and biobehavioral reviews*, 33(6), pp.807–817.

Nelson, B. et al., 2008. The phenomenological critique and self-disturbance: implications for ultra-high risk ("prodrome") research. *Schizophrenia bulletin*, 34(2), pp.381–392.

Nelson, B., Thompson, A. & Yung, A.R., 2012. Basic self-disturbance predicts psychosis onset in the ultra high risk for psychosis "prodromal" population. *Schizophrenia bulletin*, 38(6), pp.1277–1287.

Nelson, B., Thompson, A. & Yung, A.R., 2013. Not all first-episode psychosis is the same: preliminary evidence of greater basic self-disturbance in schizophrenia spectrum cases. *Early intervention in psychiatry*, 7(2), pp.200–204.

Nelson, B., Thompson, A., Chanen, A.M., et al., 2013. Is basic self-disturbance in ultra-high risk for psychosis ("prodromal") patients associated with borderline personality pathology? *Early intervention in psychiatry*, 7(3), pp.306–310.

Nelson, B., Whitford, T.J., Lavoie, S. & Sass, L.A., 2014a. What are the neurocognitive correlates of basic self-disturbance in schizophrenia? Integrating phenomenology and neurocognition: Part 2 (aberrant salience). *Schizophrenia research*, 152(1), pp.20–27.

Nelson, B., Whitford, T.J., Lavoie, S. & Sass, L.A., 2014b. What are the neurocognitive correlates of basic self-disturbance in schizophrenia?: Integrating phenomenology and neurocognition. Part 1 (Source monitoring deficits). *Schizophrenia research*, 152(1), pp.12–19.

Noë, A., 2004. *Action in Perception*, MIT Press.

Nordgaard, J. & Parnas, J., 2014. Self-disorders and the Schizophrenia Spectrum: A Study of 100 First Hospital Admissions. *Schizophrenia bulletin*, 40(6), pp.1300–1307.

Nordgaard, J., Sass, L.A. & Parnas, J., 2013. The psychiatric interview: validity, structure, and subjectivity. *European archives of psychiatry and clinical neuroscience*, 263(4), pp.353–364.

Northoff, G. et al., 2006. Self-referential processing in our brain—A meta-analysis of imaging studies on the self. *NeuroImage*, 31(1), pp.440–457.

Nygård, M. et al., 2012. Patients with Schizophrenia Fail to Up-Regulate Task-Positive and Down-Regulate Task-Negative Brain Networks: An fMRI Study Using an ICA Analysis Approach. *Frontiers in Human Neuroscience*, 6.

Olsen, K.A. & Rosenbaum, B., 2006. Prospective investigations of the prodromal state of schizophrenia: review of studies. *Acta Psychiatrica Scandinavica*, 113(4), pp.247–272.

Parnas, J., 2005. Clinical detection of schizophrenia-prone individuals: critical appraisal. *The British journal of psychiatry. Supplement*, 48(48), pp.s111–2.

Parnas, J. & Henriksen, M.G., 2014. Disordered Self in the Schizophrenia Spectrum. *Harvard Review of Psychiatry*, 22(5), pp.251–265.

Parnas, J. et al., 2003. Anomalies of subjective experience in schizophrenia and psychotic bipolar illness. *Acta Psychiatrica Scandinavica*, 108(2), pp.126–133.

Parnas, J. et al., 2011. Self-experience in the early phases of schizophrenia: 5-year follow-up of the Copenhagen Prodromal Study. *World psychiatry : official journal of the World Psychiatric Association (WPA)*, 10(3), pp.200–204.

Parnas, J. et al., 1998. Self-experience in the prodromal phases of schizophrenia: A pilot study of first-admissions. *Neurol Psychiatry Brain Res*, 6(2), pp.97–106.

Parnas, J., Carter, J. & Nordgaard, J., 2014. Premorbid self-disorders and lifetime diagnosis in the schizophrenia spectrum: a prospective high-risk study. *Early intervention in psychiatry*, 10(1), pp.45–53.

Parnas, J., Handest, P., et al., 2005. Anomalous subjective experience among first-admitted schizophrenia spectrum patients: empirical investigation. *Psychopathology*, 38(5), pp.259–267.

Parnas, J., Innocenti, G.M. & Bovet, P., 1996. Schizophrenic trait features, binding, and cortico-cortical connectivity: A neurodevelopmental pathogenetic hypothesis. *Neurol Psychiatry Brain Res*, 4(4), pp.185–196.

Parnas, J., Moller, P., et al., 2005. EASE: Examination of Anomalous Self-Experience. *Psychopathology*, 38(5), pp.236–258.

Parnas, J., Møller, P., et al., 2005. EASE: Examination of Anomalous Self-Experience. *Psychopathology*, 38(5), pp.236–258.

Parnas, J., Sass, L.A. & Zahavi, D., 2008. Recent developments in philosophy of psychopathology. *Current Opinion in Psychiatry*, 21(6), pp.578–584.

Parnas, J., Sass, L.A. & Zahavi, D., 2013. Rediscovering Psychopathology: The Epistemology and Phenomenology of the Psychiatric Object. *Schizophrenia bulletin*, 39(2), pp.270–277.

Phillips, W.A. & Silverstein, S.M., 2003. Convergence of biological and psychological perspectives on cognitive coordination in schizophrenia. *Behavioral and Brain Sciences*, 26(01), pp.65–82.

Piaget, J. & Inhelder, B., 2008. *The Psychology Of The Child*, Basic Books.

Postmes, L. et al., 2014. Schizophrenia as a self-disorder due to perceptual incoherence. *Schizophrenia research*, 152(1), pp.41–50.

Prince, M., 2015. *The Dissociation of a Personality*,

Proust, M., 2003. *In Search of Lost Time*, Penguin UK.

Putnam, F.W., 1989. Pierre Janet and modern views of dissociation. *Journal of Traumatic Stress*, 2(4), pp.413–429.

Qin, P. & Northoff, G., 2011. How is our self related to midline regions and the default-mode network? *NeuroImage*, 57(3), pp.1221–1233.

Raballo, A., 2012. Self-disorders and the experiential core of schizophrenia spectrum

vulnerability. *Psychiatria Danubina*, 24 Suppl 3, pp.S303–10.

Raballo, A. & Parnas, J., 2012. Examination of Anomalous Self-Experience. *The Journal of nervous and mental disease*, 200(7), pp.577–583.

Raballo, A. & Parnas, J., 2011. The silent side of the spectrum: schizotypy and the schizotaxic self. *Schizophrenia bulletin*, 37(5), pp.1017–1026.

Raballo, A., Sæbye, D. & Parnas, J., 2011. Looking at the schizophrenia spectrum through the prism of self-disorders: an empirical study. *Schizophrenia bulletin*, 37(2), pp.344–351.

Rappe, S., 2007. *Reading Neoplatonism*, Cambridge University Press.

Ratcliffe, M., 2008. *Feelings of Being*, Oxford University Press.

Reil, J.C. & Hübner, C.F., 1794. *Caenesthesis*, Halle.

Riecher-Rössler, A. et al., 2008. Das Basel Screening Instrument für Psychosen (BSIP): Entwicklung, Aufbau, Reliabilität und Validität. *Fortschritte der Neurologie · Psychiatrie*, 76(4), pp.207–216.

Riecher-Rössler, A. et al., 2007. The Basel early-detection-of-psychosis (FEPSY)-study ? design and preliminary results. *Acta Psychiatrica Scandinavica*, 115(2), pp.114–125.

Riva, G., Waterworth, J. & Murray, D., 2014. *Interacting with Presence*, Walter de Gruyter GmbH & Co KG.

Rochat, P., 2009. *The Infant's World*, Harvard University Press.

Roiser, J.P. et al., 2013. Neural and behavioral correlates of aberrant salience in individuals at risk for psychosis. *Schizophrenia bulletin*, 39(6), pp.1328–1336.

Röhricht, F. & Priebe, S., 2002. Do cenesthesias and body image aberration characterize a subgroup in schizophrenia? *Acta Psychiatrica Scandinavica*, 105(4), pp.276–282.

Rössler, W. et al., 2005. Size of burden of schizophrenia and psychotic disorders. *European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology*, 15(4), pp.399–409.

Ruhrmann, S. et al., 2010. Prediction of Psychosis in Adolescents and Young Adults at High Risk. *Archives of general psychiatry*, 67(3), pp.241–251.

Sandbach, F.H., 1989. *The Stoics*, Hackett Publishing.

Sartre, J.-P., 1943. *L'être et le néant*,

Sass, L., 2013. Varieties of Self-Experience: A Comparative Phenomenology of Melancholia, Mania, and Schizophrenia, Part I.

Sass, L. & Byrom, G., 2015. Phenomenological and neurocognitive perspectives on delusions: A critical overview. *World psychiatry : official journal of the World Psychiatric Association (WPA)*, 14(2), pp.164–173.

Sass, L. & Pienkos, E., 2015. Faces of Intersubjectivity. *Journal of Phenomenological Psychology*, 46(1), pp.1–32.

Sass, L., Parnas, J. & Zahavi, D., 2011. Phenomenological Psychopathology and Schizophrenia: Contemporary Approaches and Misunderstandings. *Philosophy, Psychiatry, & Psychology*, 18(1), pp.1–23.

Sass, L., Pienkos, E. & Nelson, B., 2013. Introspection and schizophrenia: a comparative investigation of anomalous self experiences. *Consciousness and cognition*, 22(3), pp.853–867.

Sass, L., Pienkos, E., Nelson, B., et al., 2013. Anomalous self-experience in depersonalization and schizophrenia: a comparative investigation. *Consciousness and cognition*, 22(2), pp.430–441.

Sass, L.A., 2003. "Negative symptoms," schizophrenia, and the self. *International journal of psychology and psychological therapy*, 3(2), pp.153–180.

Sass, L.A., 1992. *Madness and modernism*, Basic Books.

Sass, L.A., 2004. Schizophrenia: A Disturbance of the Thematic Field. In *Gurwitsch's Relevancy for Cognitive Science*. Contributions to Phenomenology. Dordrecht: Springer Netherlands, pp. 59–78.

Sass, L.A., 2014. Self-disturbance and schizophrenia: structure, specificity, pathogenesis (Current issues, New directions). *Schizophrenia research*, 152(1), pp.5–11.

Sass, L.A. & Borda, J.P., 2015. Phenomenology and neurobiology of self disorder in schizophrenia: Secondary factors. *Schizophrenia research*, 169(1-3), pp.474–482.

Sass, L.A. & Parnas, J., 2003. Schizophrenia, consciousness, and the self. *Schizophrenia bulletin*, 29(3), pp.427–444.

Saxe, G.N. et al., 1993. Dissociative disorders in psychiatric inpatients. *American Journal of Psychiatry*, 150(7), pp.1037–1042.

Scharfetter, C., 1981. Ego-psychopathology: the concept and its empirical evaluation. *Psychological medicine*, 11(2), pp.273–280.

Scharfetter, C., 1995. *The Self-experience of Schizophrenics*,

Schenkel, L. & Silverstein, S., 2004. Dimensions of Premorbid Functioning in Schizophrenia: A Review of Neuromotor, Cognitive, Social, and Behavioral Domains. *Genetic, Social, and General Psychology Monographs*, 130(3), pp.241–272.

Schneider, K., 1959. Clinical psychopathology. (5th ed.) (Trans. by M. W. Hamilton).

Schultze-Lutter, F. et al., 2013. "A rose is a rose is a rose," but at-risk criteria differ. *Psychopathology*, 46(2), pp.75–87.

Schultze-Lutter, F., Addington, J., et al., 2007. *Schizophrenia Proneness Instrument, Adult Version (SPI-A)*, Rome: Giovanni Fiorito Editore.

Schultze-Lutter, F., Marshall, M. & Koch, E., 2012. *Schizophrenia Proneness Instrument Child and Youth (SPI-CY)*,

Schultze-Lutter, F., Ruhrmann, S., et al., 2012. Basic symptoms and the prediction of first-episode psychosis. *Current pharmaceutical design*, 18(4), pp.351–357.

Schultze-Lutter, F., Ruhrmann, S., et al., 2007. The initial prodrome of schizophrenia: different duration, different underlying deficits? *Comprehensive psychiatry*, 48(5), pp.479–488.

Schwabe, L. & Blanke, O., 2007. Cognitive neuroscience of ownership and agency. *Consciousness and cognition*, 16(3), pp.661–666.

Serra, L. et al., 2007. Psychogenic and Organic Amnesia. A Multidimensional Assessment of Clinical, Neuroradiological, Neuropsychological and Psychopathological Features. *Behavioural Neurology*, 18(1), pp.53–64.

Sierra, M. & Berrios, G.E., 1997. Depersonalization: a conceptual history. *History of Psychiatry*, 8(30), pp.213–229.

Sierra, M. & Berrios, G.E., 2000. The Cambridge Depersonalization Scale: a new instrument for the measurement of depersonalization. *Psychiatry research*, 93(2), pp.153–164.

Sierra, M. & Berrios, G.E., 2001. The phenomenological stability of depersonalization: comparing the old with the new. *The Journal of nervous and mental disease*, 189(9), pp.629–636.

Sierra, M. & David, A.S., 2011. Depersonalization: A selective impairment of self-awareness. *Consciousness and cognition*, 20(1), pp.99–108.

Sierra, M. et al., 2012. Depersonalization disorder and anxiety: a special relationship? *Psychiatry research*, 197(1-2), pp.123–127.

Silveira, C., Marques-Teixeira, J. & de Bastos-Leite, A.J., 2012. More Than One Century of Schizophrenia. *The Journal of nervous and mental disease*, 200(12), pp.1054–1057.

Silverstein, S.M., Moghaddam, B. & Wykes, T., 2014. Research strategies and priorities to improve the lives of people with schizophrenia: executive summary of the Ernst Strüngmann Forum on schizophrenia. *Schizophrenia bulletin*, 40(2), pp.259–265.

Simeon, D. & Abugel, J., 2008. *Feeling Unreal: Depersonalization Disorder and the Loss of the Self*, Oxford University Press.

Simeon, D. et al., 2008. De-constructing depersonalization: further evidence for symptom clusters. *Psychiatry research*, 157(1-3), pp.303–306.

Simeon, D. et al., 1997. Feeling unreal: 30 cases of DSM-III-R depersonalization disorder. *American Journal of Psychiatry*, 154(8), pp.1107–1113.

Smieskova, R. et al., 2010. Neuroimaging predictors of transition to psychosis—A systematic review and meta-analysis. *Neuroscience and biobehavioral reviews*, 34(8),

pp.1207–1222.

Stanghellini, G., 2004. *Disembodied Spirits and Deanimated Bodies*, Oxford University Press.

Stanghellini, G., 2009a. Embodiment and schizophrenia. *World psychiatry : official journal of the World Psychiatric Association (WPA)*, 8(1), pp.56–59.

Stanghellini, G., 2013. Embodiment and schizophrenia. *World psychiatry : official journal of the World Psychiatric Association (WPA)*, 8(1), pp.56–59.

Stanghellini, G., 2009b. *Psicopatologia del senso comune*, Milano: Oxford University Press.

Stanghellini, G. & Ballerini, M., 2007. Values in persons with schizophrenia. *Schizophrenia bulletin*, 33(1), pp.131–141.

Stanghellini, G. & Fusar-Poli, P., 2012. The Vulnerability to Schizophrenia Mainstream Research Paradigms and Phenomenological Directions. *Current pharmaceutical design*.

Stanghellini, G. et al., 2012. Abnormal bodily experiences may be a marker of early schizophrenia? *Current pharmaceutical design*, 18(4), pp.392–398.

Stanghellini, G. et al., 2015. Psychopathology of Lived Time: Abnormal Time Experience in Persons With Schizophrenia. *Schizophrenia bulletin*, p.sbv052.

Stanghellini, G., Ballerini, M. & Cutting, J., 2014. Abnormal Bodily Phenomena questionnaire. *Journal of Psychopathology*, 20, pp.138–143.

Stanghellini, G., Ballerini, M., Blasi, S., et al., 2014. The bodily self: a qualitative study of abnormal bodily phenomena in persons with schizophrenia. *Comprehensive psychiatry*, 55(7), pp.1703–1711.

Stanghellini, G., Bolton, D. & Fulford, W.K.M., 2013. Person-centered psychopathology of schizophrenia: building on Karl Jaspers“ understanding of patient”s attitude toward his illness. *Schizophrenia bulletin*, 39(2), pp.287–294.

Steinberg, M., Rounsaville, B. & Cicchetti, D.V., 1990. The Structured Clinical Interview for DSM-III-R Dissociative Disorders: preliminary report on a new diagnostic instrument. *American Journal of Psychiatry*, 147(1), pp.76–82.

Stern, D.N., 1998. *The Interpersonal World of the Infant*, Karnac Books.

Stone, J., 2009. Imaging the Glutamate System in Humans: Relevance to Drug Discovery for Schizophrenia. *Current pharmaceutical design*, 15(22), pp.2594–2602.

Storring, G., 1940. Wesen und bedeutung des symptoms der ratlosigkeit bei psychischen erkrankungen. *The Journal of nervous and mental disease*, 90(6), p.798.

Störring, G., 1987. Perplexity. In *The Clinical roots of the schizophrenia concept*. Cambridge: Cambridge University Press, pp. 79–82.

Sørensen, H.J. et al., 2010. Early developmental milestones and risk of schizophrenia: A 45-year follow-up of the Copenhagen Perinatal Cohort. *Schizophrenia research*, 118(1-3), pp.41–47.

Tandon, R., 2014. Schizophrenia and Other Psychotic Disorders in Diagnostic and Statistical Manual of Mental Disorders (DSM)-5: Clinical Implications of Revisions from DSM-IV. *Indian journal of psychological medicine*, 36(3), pp.223–225.

Tandon, R., Nasrallah, H.A. & Keshavan, M.S., 2009. Schizophrenia, "just the facts" 4. Clinical features and conceptualization. *Schizophrenia research*, 110(1-3), pp.1–23.

Taylor, J.G., 2011. A neural model of the loss of self in schizophrenia. *Schizophrenia bulletin*, 37(6), pp.1229–1247.

Thompson, E., 2007. *Mind in Life*, Harvard University Press.

Tsakiris, M., 2010. My body in the brain: A neurocognitive model of body-ownership. *Neuropsychologia*, 48(3), pp.703–712.

Tsakiris, M., Costantini, M. & Haggard, P., 2008. The role of the right temporo-parietal junction in maintaining a coherent sense of one's body. *Neuropsychologia*, 46(12), pp.3014–3018.

Tsakiris, M., Schütz-Bosbach, S. & Gallagher, S., 2007. On agency and body-ownership: Phenomenological and neurocognitive reflections. *Consciousness and cognition*, 16(3), pp.645–660.

Tyrer, P. & Kendall, T., 2009. The spurious advance of antipsychotic drug therapy. *The Lancet*, 373(9657), pp.4–5.

Uhlhaas, P.J. & Mishara, A.L., 2007. Perceptual anomalies in schizophrenia: integrating phenomenology and cognitive neuroscience. *Schizophrenia bulletin*, 33(1), pp.142–156.

Uhlhaas, P.J. & Silverstein, S.M., 2005. Perceptual Organization in Schizophrenia Spectrum Disorders: Empirical Research and Theoretical Implications. *Psychological Bulletin*, 131(4), pp.618–632.

van den Bos, E. & Jeannerod, M., 2002. Sense of body and sense of action both contribute to self-recognition. *Cognition*, 85(2), pp.177–187.

van der Meer, L. et al., 2010. Self-reflection and the brain: A theoretical review and meta-analysis of neuroimaging studies with implications for schizophrenia. *Neuroscience and biobehavioral reviews*, 34(6), pp.935–946.

Varela, F.J., 1993. *The Embodied Mind*, Mit Press.

Velthorst, E. et al., 2009. Baseline differences in clinical symptomatology between ultra high risk subjects with and without a transition to psychosis. *Schizophrenia research*, 109(1-3), pp.60–65.

Velthorst, E. et al., 2010. Disability in people clinically at high risk of psychosis. *The*

British journal of psychiatry : the journal of mental science, 197(4), pp.278–284.

Waller, N., Putnam, F.W. & Carlson, E.B., 1996. Types of dissociation and dissociative types: A taxometric analysis of dissociative experiences. *Psychological Methods*, 1(3), pp.300–321.

Waller, N.G. & Ross, C.A., 1997. The prevalence and biometric structure of pathological dissociation in the general population: Taxometric and behavior genetic findings. *Journal of abnormal psychology*, 106(4), pp.499–510.

Winton-Brown, T.T. et al., 2014. Dopaminergic basis of salience dysregulation in psychosis. *Trends in Neurosciences*, 37(2), pp.85–94.

Woodberry, K.A., M.S.W., A., Giuliano, A.J., Ph.D. & Seidman, L.J., Ph.D., 2008. Premorbid IQ in Schizophrenia: A Meta-Analytic Review. *American Journal of Psychiatry*, 165(5), pp.579–587.

World Health Organization, 1992. *The ICD-10 Classification of Mental and Behavioural Disorders*, Diamond Pocket Books (P) Ltd.

Wylie, K.P. & Tregellas, J.R., 2010. The role of the insula in schizophrenia. *Schizophrenia research*, 123(2-3), pp.93–104.

Wyllie, M., 2005. Lived Time and Psychopathology. *Philosophy, Psychiatry, & Psychology*, 12(3), pp.173–185.

Yung, A.R. & McGorry, P.D., 1996. The initial prodrome in psychosis: descriptive and qualitative aspects. *The Australian and New Zealand journal of psychiatry*, 30(5), pp.587–599.

Yung, A.R. et al., 2005. Mapping the onset of psychosis: the Comprehensive Assessment of At-Risk Mental States. *The Australian and New Zealand journal of psychiatry*, 39(11-12), pp.964–971.

Yung, A.R. et al., 1996. Monitoring and Care of Young People at Incipient Risk of Psychosis. *Schizophrenia bulletin*, 22(2), pp.283–303.

Yung, A.R. et al., 2006. Testing the Ultra High Risk (prodromal) criteria for the prediction of psychosis in a clinical sample of young people. *Schizophrenia research*, 84(1), pp.57–66.

Zahavi, D., 2000. *Exploring the self: Philosophical and psychopathological perspectives on self-experience*, John Benjamins Publishing.

Zahavi, D., 2014. *Self and Other*, Oxford University Press, USA.

Zahavi, D., 1999. *Self-awareness and Alterity*, Northwestern University Press.

Zahavi, D., 2008. *Subjectivity and Selfhood*, MIT Press.

Zahorik, P. & Jenison, R.L., 1998. Presence as Being-in-the-World. *Presence: Teleoperators and Virtual Environments*, 7(1), pp.78–89.